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## Case Report

# Gynecomastia in a Transgender Boy: A Case Report

Raymond Fung, MD, BSc, FRCPC<sup>1,\*</sup>,  
Mary Kathleen Greenaway, MD, BSc, MPH, CCFP, FCFP<sup>2</sup>, Giancarlo McEvenue, MD, FRCSC<sup>3</sup>

<sup>1</sup> Division of Endocrinology, Department of Medicine, Michael Garron Hospital, University of Toronto, Toronto, Canada

<sup>2</sup> University of Toronto, Toronto, Canada

<sup>3</sup> McLean Clinic, Mississauga, Ontario, Canada

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## ABSTRACT

**Objective:** To describe the case of a 17-year-old transgender boy who experienced breast development while on testosterone, having been suppressed with a gonadotropin-releasing hormone (GnRH) agonist prior to testosterone therapy

**Case report:** A 17-year-old transgender boy presented with breast development after having been on a GnRH agonist and then testosterone since the age of 11 years, having never experienced breast development before, which was consistent with pubertal gynecomastia. A small decrease in the testosterone dose resulted in a significant reduction of gynecomastia. Despite the improvement, he went on to undergo chest surgery with the removal of the breast tissue.

**Discussion:** Pubertal gynecomastia is a common phenomenon in the cisgender male population. However, it has not been previously described in transgender boys. The potential mechanisms for its occurrence were discussed.

**Conclusion:** Transgender boys who undergo GnRH agonist treatment for puberty suppression and subsequently receive testosterone therapy for puberty induction may develop gynecomastia. Judicious adjustment of the testosterone therapy may lead to an improvement.

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## Introduction

0.5% to 1% of various populations around the world identify as transgender.<sup>1</sup> Gonadotropin-releasing hormone agonists (GnRH) have been used to suppress puberty in transgender boys (assigned female at birth who identify as male) to halt breast development, starting at Tanner stage 2.<sup>2</sup> Testosterone is subsequently used to induce male puberty, with expected effects such as lowering of the voice, increased lean muscle mass, increased body and facial hair as well as decrease in breast glandular tissue.<sup>2</sup> We report an unexpected effect of testosterone therapy.

## Case Report

A 17-year-old transgender boy was referred to an endocrinology clinic for gynecomastia. Informed consent was obtained from the patient.

*Abbreviations:* GnRH, gonadotropin-releasing hormone; IM, intramuscular.

\* Address correspondence and reprint requests to Dr Raymond Fung, 650 Sammon Avenue, K 302, Toronto, ON, Canada, M4C 5M5.

E-mail address: [Raymond.fung@tehn.ca](mailto:Raymond.fung@tehn.ca) (R. Fung).

He identified as a boy since childhood, and at the age of 11 years, he was started on a gonadotropin-releasing hormone (GnRH) agonist for puberty suppression. Since the initiation of the GnRH agonist therapy, he did not experience any breast development nor menses. At the age of 14 years, he was started on 50 mg of testosterone cypionate intramuscularly (IM) every 2 weeks, which was gradually increased to 80 mg IM every 2 weeks. At that point, the GnRH agonist therapy was stopped, and he continued to do well with masculinizing changes, without experiencing any menses.

Nine months prior to the presentation, his testosterone dose was increased to 100 mg IM every 2 weeks. Four months prior to the presentation, he started to notice bilateral lumpy breast growth, which was tender, with the left side more tender than the right. The growth continued, and 3 months prior to presentation, he noticed a bloody discharge from the left nipple with light squeezing. Two months prior to the presentation, he was assessed by a general surgeon, and an ultrasound was performed, which showed normal-appearing bilateral breast tissue, with no concerning nodule or cyst. At around the same time, he was advised to decrease his testosterone dose from 100 mg back to 80 mg every 2 weeks. Three to 4 weeks after

decreasing his dose, the bleeding from his left nipple stopped, breast swelling decreased, and tenderness resolved.

His past medical history included a learning disability, attention-deficit hyperactive disorder, mild asthma, and depression. In addition to the testosterone, he was taking 15 mg of vortioxetine daily and salbutamol as needed. He smoked cigarettes, 1 pack every 3 days. He stopped smoking marijuana 2 years prior to the presentation and occasionally consumed alcohol.

On examination, he was a slender, healthy-looking, young man. His height was 164 cm, weight was 53.6 kg, and body mass index was 19.9 kg/m<sup>2</sup>. The pitch of his voice was in the male range, and he had some scant facial hair, with mild facial acne. Respiratory and cardiac examination results were unremarkable. The left side of his chest was slightly larger than the right, with minimal breast tissue palpable. There was no tenderness and nipple abnormality. This corresponds to the spontaneous improvement that he reported after the decrease in the testosterone dose.

**Investigations**

Prior to the increase in the testosterone dose, 10 months before the presentation, his total testosterone level was 17.5 nmol/L (504 ng/dL) (Table 1). One month after the onset of breast growth, his total testosterone level was 29.4 nmol/L (847 ng/dL) (range, 8–28 nmol/L) and estradiol level was 113 pmol/L (32.6 pg/mL). The testosterone levels were measured 1 week after the injection (midcycle). His complete blood count and creatinine, aspartate aminotransferase, alanine aminotransferase, thyroid-stimulating hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, alpha fetoprotein, and beta human chorionic gonadotropin levels were in the normal range. After his dose was decreased, his testosterone level (1 week after the injection) declined to 13.0 nmol/L (375 ng/dL), and his estradiol level at that time was 161 pmol/L (46.4 ng/dL).

**Subsequent Course and Surgery**

The patient continued to experience significant dysphoria with the remaining breast tissue and was, therefore, referred to the plastic surgery department. At the time of the plastic surgery consultation, the patient was noted to have good muscular development in his chest, bilateral grade-1 breast ptosis with a small amount of breast tissue, and no excess skin. Subcutaneous mastectomy via a periareolar incision was recommended to the patient. This technique was used to provide an optimum chest contour and for the removal of adipose and breast tissue while minimizing scar burden.

**Table 1**  
Total Testosterone and Estradiol Levels in Relation to the Patient’s Testosterone Level and Onset of Gynecomastia

Hormone Level	Prior to the Onset of Gynecomastia, on 80 mg of Testosterone Every 2 wk	One Month After the Onset of Gynecomastia, on 100 mg of Testosterone Every 2 wk	Three Months After a Decrease in Testosterone Dose Back to 80 mg Every 2 wk
Total testosterone level in nmol/L (ng/dL)	17.5 (504)	29.4 (847)	13.0 (375)
Estradiol level in nmol/L (pg/mL)		113 (32.6)	161 (46.4)

The testosterone levels were measured 1 week after injection (midcycle).

During his surgery, 2 breast tissue specimens were removed and sent for pathologic assessment. The right specimen measured 7 × 5 × 2.2 cm and weighed 20 g; the left specimen measured 8 × 6 × 2.3 cm and weighed 27 g, and both were identified as breast tissue. At 1-year follow up postoperatively, there were no complications or need for revisions. There were no further episodes of bloody discharge noted by the patient. The patient declined photographs to be taken.

**Discussion**

Gynecomastia is the benign proliferation of the male breast glandular tissue. Its pathophysiology is thought to be due to an imbalance in the androgenic and estrogenic effects on breast tissue, although the exact etiology is still unclear.<sup>3</sup> Conditions that lead to relative excess estrogen effects on the breast tissue, over the inhibiting effects of androgens, can lead to gynecomastia.<sup>3</sup> The enhanced sensitivity of the breast tissue to normal concentrations of estrogen and androgens might also play a role.<sup>4</sup>

Physiologic gynecomastia occurs in the neonatal period, during puberty, and during senescence. Pubertal gynecomastia has a peak occurrence in individuals aged between 13 and 14 years, when the Tanner stage 3 to 4 of sexual development is reached. The reported incidence varies widely, with up to 70% of boys reported to experience gynecomastia during puberty in some publications.<sup>4</sup> In the vast majority (90%) of pubertal gynecomastia spontaneously regresses in 6 months to 3 years.<sup>5</sup> If it persists for >1 year, the tissue is more likely to become fibrotic and regression is much less likely. Surgical management may be appropriate in those who have psychological distress associated with persistent gynecomastia, with positive results reported, including an improvement in quality-of-life measures.<sup>6,7</sup>

The secondary causes of gynecomastia include medications; chronic liver or kidney disease; hypogonadism; hyperthyroidism; and malignancy (including human chorionic gonadotropin tumors; Leydig, Sertoli, and granulosa cell testicular tumors; as well as estrogen-secreting adrenal tumors).<sup>8</sup>

The management of pubertal gynecomastia is tailored to individual patients. Because of the high rate of spontaneous remission, conservative follow up is recommended for those who are not distressed by their condition.<sup>5</sup> Pharmacologic management may be tried for those with significant symptoms. These agents include tamoxifen (blocking estrogen receptor in the mammary epithelium) and aromatase inhibitors (inhibiting estrogen production). Tamoxifen may have moderate effectiveness when given early in the course, although the evidence is limited to small studies with methodologic flaws.<sup>5</sup> In a study of the aromatase inhibitor anastrozole, no difference was found between the effectiveness of anastrozole and placebo.<sup>9</sup>

We report a case of gynecomastia in a transgender boy undergoing the induction of puberty with exogenous testosterone therapy. He was started on GnRH agonist therapy for puberty suppression very early and had experienced little, if any, female pubertal development. He did not report any significant breast development prior to puberty suppression (in contrast to the current recommended guidelines). It was 3 years into this testosterone therapy, when the dose was increased, that he experienced breast growth. The peak incidence of pubertal gynecomastia occurs about 3 years after the onset of puberty, which is similar to the duration for which this patient was on exogenous testosterone prior to the onset of gynecomastia.

After the dose was increased, we hypothesized that there had been an increased conversion from testosterone to estrogen, resulting in gynecomastia, although we were unable to prove this with the hormone level tests that we obtained. Other than the

imprecision of the estradiol assay and/or timing of the test, we cannot explain why the estradiol level, after the testosterone dose was decreased, was actually higher. The patient's gynecomastia improved shortly after a decrease in the testosterone dose, which supports our hypothesis. Another theory for pubertal gynecomastia is that his breast tissue had enhanced sensitivity to estrogen stimulation, with increased aromatization of androgens to estrogens by the breast tissue itself.<sup>5</sup> Increased aromatase activity has been found in pubic skin fibroblasts of patients with gynecomastia.<sup>10</sup>

An atypical feature of this case was the unilateral bloody nipple discharge that the patient experienced, with no underlying pathology found, which also spontaneously resolved as the gynecomastia improved. No secondary causes of gynecomastia were found. We did not find an association between vortioxetine and gynecomastia.

### Conclusion

With the increasing numbers of transgender youth presenting for puberty suppression and subsequent cross-sex hormone therapy, we expect that there may be more cases of gynecomastia associated with testosterone pubertal induction. The small increase in the testosterone dose may have been a precipitant factor in this case. This case highlights the importance of the careful adjustment of testosterone dose, which may play a role in preventing the occurrence of this phenomenon. Further research on the potential mechanisms may shed light on how to best prevent this condition from occurring during testosterone puberty induction.

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### Disclosure

The authors have no multiplicity of interest to disclose.

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