Oocyte cryopreservation in a transgender man on long-term testosterone therapy: a case report

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Objective: To report a case of ovarian stimulation for the purposes of oocyte cryopreservation in a transgender man without cessation of long-term testosterone therapy.
Design: Report of a unique case of fertility preservation through ovarian stimulation and oocyte cryopreservation in a transgender man who had been on testosterone therapy for 18 months before treatment. The patient elected to continue testosterone therapy throughout ovarian stimulation and oocyte retrieval. To our knowledge, there have not been any published reports of patients undergoing oocyte cryopreservation while continuing long-term testosterone therapy.
Setting: Private fertility clinic with university affiliation.
Patient(s): A 20-year-old transgender man undergoing oocyte cryopreservation before gonadectomy.
Intervention(s): Fertility preservation through oocyte cryopreservation.
Main Outcome Measure(s): This patient had a robust response to ovarian gonadotropin stimulation. Leuprolide acetate was used for final oocyte maturation to minimize ovarian hyperstimulation syndrome risk.
Result(s): Cryopreservation of 22 mature oocytes.
Conclusion(s): Cryopreservation of mature oocytes is possible for patients on continued long-term testosterone therapy. The impact of long-term testosterone therapy on markers of ovarian reserve, reproductive potential, and long-term reproductive outcomes have yet to be elucidated and further studies are needed in this area. (Fertil Steril Rep® 2021;2:249–51. ©2021 by American Society for Reproductive Medicine.)
Key Words: Oocyte cryopreservation, fertility preservation, ovarian stimulation, transgender men, testosterone

INTRODUCTION

There has been an exponential rise in referrals to specialist clinics for hormone treatment for gender identity, and in 2017, there were over 1,000 new referrals among 9 specialty clinics across Canada (1). Many transgender men and women express the desire to have children and would consider fertility preservation (2, 3). National and international organizations recommend a discussion about fertility preservation before gender-affirming hormone therapy or surgery (4–6).

Uptake on fertility preservation among transgender men has been low. Barriers to pursuing fertility preservation include, among others, the lack of information from their health care professionals, inadequate provider knowledge, patient unwillingness to delay the start of hormone blockers or androgen therapy, as well as the invasiveness and cost of the procedures (7–11). Case reports and series describe oocyte cryopreservation among transgender men before initiation or after discontinuation of androgen therapy (12–17).

Counseling patients regarding proceeding with fertility preservation who have already started testosterone therapy is challenging. Cessation of testosterone therapy before oocyte cryopreservation is a barrier to pursuing oocyte cryopreservation given the gender dysphoria that is often experienced with stopping testosterone. The impact of long-term testosterone therapy on the ovaries and reproductive potential is largely unknown and speculative. The reports on the effect of testosterone on the ovary at the molecular and histological level are inconclusive (18, 19).

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Patients on testosterone therapy at the time that they decide to proceed with a cycle of oocyte cryopreservation at our center are informed of the unknown effects of testosterone on the ability of the ovary to respond to gonadotropin stimulation, oocyte quality, the ability of these oocytes to fertilize, live birth rates, and potential long-term epigenetic effects. Patients are informed that given the unknown impact of testosterone, it is advised to stop the testosterone for 1–3 months before the start of ovarian stimulation (20). We present a case report of ovarian stimulation and oocyte cryopreservation in a patient on long-term testosterone therapy who elected to continue testosterone therapy throughout his oocyte cryopreservation treatment cycle.

CASE REPORT

A 20-year-old transgender man, on testosterone therapy for gender affirmation for 18 months, presented for oocyte cryopreservation. Informed consent was obtained from the patient for publication of this case report. The patient's past medical history was significant for bilateral mastectomy. His only medication was once weekly intramuscular testosterone (25 mg weekly) therapy. He was not taking leuprolide acetate for gender-affirming therapy. Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy were scheduled shortly after the completion of the oocyte cryopreservation. He did not have a partner at the time of oocyte cryopreservation.

The patient underwent the prerequisite ovarian reserve testing before ovarian stimulation. He was able to tolerate transvaginal ultrasound evaluation monitoring, and this was undertaken throughout the investigations and treatment. Baseline transvaginal ultrasound demonstrated a normal uterus and ovaries, with an antral follicle count >40. Baseline serum antimüllerian hormone level was 44 pmol/L (19.6 ng/mL).

A gonadotropin-releasing hormone (GnRH) antagonist protocol was prescribed with follitropin alfa (175 IU daily, Gonal-f; EMD Serono, Canada) and lutropin alfa (75 IU daily, Luveris; EMD Serono, Canada). He began the GnRH antagonist cetrorelix (Cetrotide; EMD Serono, Canada) on the 5th day of stimulation, at which point the estradiol serum level was measured at 3,238 pmol/L (882 pg/mL). Given a robust ovarian response to stimulation with 33 follicles measuring >13 mm average diameter, leuprolide acetate trigger (3 mg [0.6 mL]) was prescribed at 8 PM on the 9th day of stimulation, and the patient was placed on oral cabergoline (0.5 mg every 3 days; Dostinex; Pfizer, Canada) for 4 doses for prevention of ovarian hyperstimulation syndrome (OHSS). Blood tests on the morning before the evening leuprolide acetate administration demonstrated a luteinizing hormone (LH) serum level of 1 IU/L and progesterone serum level of 5.2 nmol/L (1.6 ng/mL), both of which increased on the day after leuprolide acetate administration (12.5 hours post leuprolide acetate injection) to 19 IU/L and 41.6 nmol/L (13.1 ng/mL), respectively. This confirmed a physiologic response to the leuprolide acetate administration. Transvaginal egg retrieval occurred 36 hours after the leuprolide acetate injection.

A transvaginal ultrasound-guided oocyte retrieval was undertaken under conscious sedation and 25 cumulous oocyte complexes were retrieved. Twenty-two metaphase 2 oocytes were cryopreserved through vitrification. The patient was monitored for OHSS after the procedure and developed the mild form characterized by abdominal bloating, which resolved over the following few days.

DISCUSSION

This case report demonstrated a proof of concept that undergoing a cycle of oocyte cryopreservation while continuing long-term testosterone therapy is possible. The ovarian reserve markers were predictive of the ovarian response in this case; however, the impact of testosterone on the markers of ovarian reserve is largely unknown. Some publications suggest that testosterone therapy is associated with a suppressive effect on markers of ovarian reserve, and in one study testosterone resulted in a strong suppression of antimüllerian hormone secretion over a relatively short period of 16 weeks (21).

This case also demonstrated an appropriate, however perhaps slightly blunted, physiologic response to leuprolide acetate injection for final maturation of the oocytes in the setting of long-term testosterone therapy. Given the robust response, leuprolide acetate was used to minimize the perceived risk of OHSS; however, the ability of the pituitary to mount a physiologic response after prolonged testosterone exposure was questioned. Blood tests 12.5 hours after leuprolide acetate administration confirmed a physiologic response, which was further confirmed by the retrieval of mature oocytes. We based our assessment of a minimal rise in LH serum level >15 mIU/mL and progesterone serum level >3 ng/mL on a published report documenting success with oocyte retrieval with LH levels 10.8 ± 2 hours after trigger above this threshold (although this patients' value was over the lower threshold, it was significantly below the mean LH response concentration of 60.2 ± 35.6 mIU/mL) (22). Further studies evaluating the response to leuprolide acetate for oocyte maturation among patients on long-term testosterone therapy are warranted.

In conclusion, given the perceived potential negative impact of either delay of the start of testosterone therapy to pursue fertility preservation or the cessation of testosterone once already commenced before the start of ovarian stimulation, the continuation of testosterone therapy throughout the fertility preservation process should be further explored. The impact of long-term testosterone therapy on the markers of ovarian reserve, ovarian response to stimulation, oocyte quality, and long-term epigenetic effect on resultant offspring are unknown. Further studies are warranted.

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