Cryopreservation after long-term testosterone therapy in the trans-male patient

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ABSTRACT

Introduction: In an era of a growing transgender population with earlier intervention of hormonal therapy, there is little scientific literature describing effects of prolonged exogenous administration of testosterone on fertility. It is now more important than ever to understand the reproductive health needs of transgender patients and the potential long term effects of hormone therapy on fertility. The following case report demonstrates the fertility preservation potential in a trans-male patient after eight years of testosterone therapy. Case Report: The patient is a 25-year-old go female to male (FTM) trans-male seeking fertility preservation. He had been taking consistent testosterone therapy since adolescence, a total of eight years prior to presentation. His last menstrual period was shortly after his hormonal therapy commenced. The patient was instructed to stop his testosterone therapy. Onset of menses occurred six weeks later. He started combined Oral Contraceptive Pills (OCPs) for ovulation suppression for seven days. Controlled ovarian stimulation was then initiated with home injections of Follistim (Ravensburg, Germany) and Menopur (Parsippany, NJ) for 11 days. Ganarelix (Ravensburg, Germany) was started on day-9 of stimulation. On day-11, his estradiol (E2) was 1339 pg/mL, there were nine follicles >16 mm and 10 follicles <16 mm. HCG trigger was administered. His egg retrieval procedure 36 hours later yielded 22 oocytes, 18 of which were mature and vitrified. Conclusion: This case demonstrates that fertility is possible for the young trans-male patient, regardless of the number of years of prior testosterone therapy. Providers must develop gender-appropriate support to address reproductive goals of their transgender patients.

Keywords: Cryopreservation, Fertility preservation Transgender, Testosterone therapy, Trans male

INTRODUCTION

There is little scientific literature describing effects of prolonged exogenous administration of testosterone on fertility. Studies suggest amenorrhea commonly occurs within six months of initiating testosterone therapy, however the time frame for resumption of menses after testosterone cessation is not well documented, and some suggest that amenorrhea may be irreversible [1, 2]. The few case reports, review articles, and narratives in the
press that make up the majority of the literature we have on the subject are limited to patients who decided to undergo fertility preservation prior to initiation of gender-affirming hormone therapy [2], or patients who had previously been on testosterone therapy for 1–2 years prior to attempting cryopreservation. Our objective was to evaluate the fertility preservation potential in the trans male patient after eight years of testosterone therapy.

**CASE REPORT**

This is a case report of a 25-year-old Go female to male (FTM) trans-male seeking fertility care. His chief complaint was that he one day wanted children, and was specifically interested in cryopreservation. He had been taking “gender affirming” hormonal therapy since adolescence, a total of eight years of consistent testosterone therapy (Testosterone Cypionate 0.5 mL weekly) prior to presentation. His last menstrual period was shortly after his hormonal therapy commenced. He was sexually active with women and identified as heterosexual. He was otherwise a healthy patient with no significant medical history. His routine gynecological screening was up to date and was normal. His medication list only included Testosterone Cypionate 0.5 mL weekly.

On initial fertility work up, his AMH was 6.24 ng/mL, TSH 2.5 mIU/mL, Prolactin 8.3 ng/mL. His BMI was 22 kg/m². He was instructed to stop his Testosterone supplementation and wait for the onset of menses prior to initiating a controlled ovarian stimulation protocol.

The patient’s onset of menses ultimately occurred six weeks later after cessation of testosterone therapy. On cycle day-5, his antral follicle count (AFC) was sixteen. He then started combined OCPs for ovulation suppression for seven days. Controlled ovarian stimulation was initiated with at home injections of Follistim (Ravensburg, Germany) 250 mcg/0.5 ml, Menopur (Parsippany, NJ) 125 IU for five days and on day-6 the regimen was increased to Follistim 225 IU and Menopur 125 IU for a total stimulation of 11 days. On day number nine of stimulation, Ganarelix (Ravensburg, Germany) 250 mcg/0.5 ml was started. The stimulation period was uncomplicated with minimal side effects. On day-11, there were no follicles >16 mm and ten follicles <16 mm. HCG trigger was administered. His Estradiol (E2) level on day of HCG trigger was 1339 pg/mL. He underwent an egg retrieval procedure 36 hours later and twenty two oocytes were retrieved, eighteen of which were mature and vitrified. Following the retrieval procedure, he resumed his testosterone therapy.

**DISCUSSION**

Despite the growing acceptance of Assisted Reproductive Technologies (ART) for the Transgender population, the reproductive effects of long term testosterone therapy in transgender men remains largely unknown. The literature available including observational studies and small retrospective studies demonstrate successful cryopreservation in trans male patients prior to initiating gender reaffirming therapy and in patients who been on testosterone for 1-2 years prior to cryopreservation.

To our knowledge, this is the first case report documenting successful oocyte cryopreservation in a transgender male after 8 years of testosterone therapy. Not only was this treatment successful, his response to treatment was almost immediate. To our surprise, this patient had resumption of menses within six weeks of stopping his gender affirming hormonal therapy and responded to ovarian stimulation immediately, yielding multiple mature oocytes for cryopreservation after one cycle.

According to Light et al., in their small observational study looking at pregnancy in transgender men, 84% of patients who achieved a live birth were on testosterone therapy prior to attempting pregnancy and were able to achieve pregnancy using their own eggs. Total 32% of patients conceived while on testosterone therapy. They also reported that participants who discontinued testosterone to attempt pregnancy reported resumption of menses within six months. This conclusion was consistent with that of literature on women who became amenorrheic with testosterone producing Sertoli-Leydig tumors and resumed menstruation after tumor resection [3]. Additional research has demonstrated that even in amenorrheic patients secondary to exogenous testosterone therapy, the ovarian follicle pool is not affected, suggesting that ovarian stimulation for cryopreservation is likely possible despite prolonged testosterone therapy [4].

Additional qualitative studies have demonstrated that about 50% of transgender adults desire to have children and about 40% of trans male patients would consider cryopreservation.

Interestingly, qualitative studies in transgender adolescents have demonstrated that only 25% of patients report a desire to have children in the future, which, not surprisingly suggests that as these children mature through their reproductive years, many patients change their mind in regards to their desire to reproduce [5]. Thus, the American Society for Reproductive Medicine (ASRM) recommends that providers should offer fertility preservation options to individuals before gender transition. Patients should be counseled regarding the lack of data on medical and psychosocial risks associated with ART in the transgender population, including the lack of information known regarding outcomes for patients who have been on long term testosterone therapy [6]. For those patients who change their mind and/or did not receive initial counseling, this case report offers some hope that in some otherwise healthy trans male patients, fertility may be preserved despite long term testosterone therapy.
CONCLUSION

This case demonstrates that fertility is possible for the young trans-male patient, regardless of the number of years of prior testosterone therapy. Providers must develop gender-appropriate support to address reproductive goals of their transgender patients. It is important for transgender patients to be aware that there is a lack of data regarding the medical and psychological risks pertaining to ART in this population and that further evidence-based research is needed to understand the long term impact and outcomes for transgender patients and their offspring.

REFERENCES


Author Contributions
Jenna Kahn – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Maureen Kelly – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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