



Contents lists available at ScienceDirect

AAACE Clinical Case Reports

journal homepage: www.aaaceclinicalcasereports.com

Case Report

Successful In Vitro Fertilization in a Cisgender Female Carrier Using Oocytes Retrieved From a Transgender Man Maintained on Testosterone

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ARTICLE INFO

Article history:

Received 4 March 2021

Received in revised form

2 June 2021

Accepted 7 June 2021

Available online 16 June 2021

Key words:

IVF

transgender

testosterone

assisted reproduction

ABSTRACT

Background: Health care providers routinely discontinue testosterone in transgender men undergoing oocyte retrieval. To date, there is little literature to support such discontinuation. The sudden drop in testosterone levels can be distressing for transgender men. The objective of this report was to describe a case study of successful reciprocal in vitro fertilization (IVF) using oocytes retrieved from a transgender man who remained on testosterone during the entire course of gonadotropin controlled ovarian stimulation and retrieval.

Case Report: A 33-year-old gravida 0 transgender man and his partner, a 42-year-old gravida 0 cisgender woman, presented to an outpatient clinic in 2017 seeking reciprocal IVF. Both patients were healthy with no significant past medical history. The transgender patient reported a 10-year history of testosterone hormone therapy. Both patients reported no other medication use. The transgender man underwent a 14-day course of ovarian stimulation before oocytes were retrieved. An oocyte was then fertilized and implanted into the uterus of the patient's cisgender female partner. The reciprocal IVF resulted in an uncomplicated, full-term pregnancy with vaginal delivery. The child is now 2 years old and developmentally normal.

Discussion: To our knowledge, this is the first report of a live birth from an oocyte retrieved from a transgender man who continued to use testosterone throughout assisted reproduction.

Conclusion: Fertility preservation options for transmasculine people may include stimulated egg retrieval if the ovaries are left in place even when the patients remain on testosterone therapy.

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Introduction

Data concerning transgender men suggest that a majority want children.¹ While the literature regarding transgender individuals and pregnancy is modest, there are reports of reproduction among transgender men.² It follows that several transgender men desire counseling about reproductive options.³ This manuscript will use field-standard terminology.⁴

Abbreviations: COS, controlled ovarian stimulation; HT, hormone therapy; IVF, in vitro fertilization.

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<https://doi.org/10.1016/j.aaace.2021.06.007>

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The majority of transgender men who start gender-affirming hormone therapy (HT) maintain their ovaries and, thus, retain their ability to produce oocytes during childbearing years.^{5–8} While the literature is sparse, prior work shows that biological reproduction can be safe and successful for transgender men even after testosterone use.^{5,6} In a survey of 41 transgender men who became pregnant, Light et al⁵ found that 25 (61%) of respondents had used testosterone before pregnancy and the vast majority (88%) used oocytes from their own ovaries. Additionally, 5 participants conceived while amenorrheic from testosterone use (however, it remains unclear whether they were still using testosterone at the time of conception). Five (25%) of the patients who had taken testosterone used assisted reproduction to get pregnant.⁶

Assisted reproduction has been a revolutionary tool for lesbian, gay, bisexual, transgender, queer/questioning people.⁹ In vitro fertilization (IVF), wherein oocytes are harvested and combined with sperm to create an embryo that is then transferred into a uterus, has been a strategy for transgender men seeking biological reproduction.^{2,6} Reciprocal, or co-IVF, is the process by which individuals provide oocytes for implantation into their cisgender partners' uteri or in other people with a uterus who agree to carry a pregnancy (also known as a gestational carrier or a surrogate). Co-IVF has been used in lesbian couples with good reproductive success.^{10,11} It has also been used with success in transgender men donating an oocyte to cisgender female partners.⁶

Little is known about the effect of testosterone on either fertility or oocyte quality. Because of this uncertainty, providers have counseled transgender men to discontinue testosterone before attempted reproduction.^{2,6,8} Notably, discontinuation of testosterone can trigger significant distress.² Therefore, questions regarding the safety and success of pregnancy in the setting of ongoing testosterone use are of high importance.

As described earlier, the literature provides evidence for the safety and success of IVF after testosterone has been initiated and paused for oocyte retrieval. However, there exists no documentation of the pregnancy outcomes of transgender men who continue to use testosterone during oocyte stimulation for reciprocal IVF. We comment on the phenomenon in this case report.

Case Report

A 33-year-old transgender man and his partner, a 42-year-old cisgender woman, presented to an outpatient clinic in 2017 seeking reciprocal IVF. The transgender man sought to provide oocytes, which were to be fertilized with donor sperm to create an embryo for his partner, who planned to carry the pregnancy. Both patients were healthy, with no significant past medical history or allergies. Neither patient took medications, except for testosterone in the case of the transgender man. Neither patient had been pregnant before. The cisgender female partner reported regular (27–28 days) menstrual cycles.

The transgender man had begun subcutaneous testosterone replacement therapy in 2007 and had been on gender-affirming HT for approximately 10 years. At the time of presentation, the patient's HT regimen consisted of 50-mg subcutaneous testosterone weekly. He reported some vaginal spotting, suggesting that his testosterone dose could have been increased. However, the patient elected to continue with his 50-mg testosterone dose during follicle stimulation for IVF. The patient had undergone chest wall surgery but no other gender-affirming surgery. Therefore, he had a uterus and both ovaries. The patient was noted to have higher-than-average ovarian reserve by means of sonographic assessment of antral follicle count as well as his serum anti-Müllerian hormone levels.

The couple elected for reciprocal IVF with intracytoplasmic sperm injection using anonymous donor sperm and preimplantation genetic testing of the embryos. The transgender man underwent a 14-day course of gonadotropin controlled ovarian stimulation (COS) at the highest dose, including 300 units of follicle-stimulating hormone (Follistim, Merck), 150 units of human menopausal gonadotropin (Menopur, Ferring), and 0.25 mg of gonadotropin-releasing hormone antagonist (ganirelix acetate, Organon), all administered daily via subcutaneous injections. On the 14th day of COS, once the standard criteria were met,¹² the final oocyte maturation was induced by subcutaneous injection of 40 units of leuprolide acetate (Lupron, Abbott Pharmaceuticals) and

1000 units of human chorionic gonadotropin. Oocytes were retrieved 36 hours later. Twenty oocytes were retrieved, 16 were mature, and 13 were fertilized via intracytoplasmic sperm injection with spermatozoa from an anonymous donor. Five embryos progressed to the blastocyst stage and were sent for preimplantation genetic testing to assess for chromosomal abnormalities. For a 33-year-old, the expected aneuploidy rate among embryos is 31%¹³; however, only one embryo was chromosomally normal, suggesting an aneuploidy rate of 80%.

One month later, the normal embryo was transferred into the partner's uterus with the default programmed embryo transfer protocol, including 10 days of oral estradiol 2 mg twice daily that started on the second day of the menstrual cycle, followed by 5 days of intramuscular progesterone administration at a dose of 50 mg daily after which an embryo transfer was performed in a usual fashion.¹⁴ She carried the pregnancy without complications and had a full-term vaginal delivery. The child is now 2 years of age and is developmentally normal.

Discussion

This is the first report of a live birth from an oocyte retrieved from a transgender man who continued to use testosterone throughout assisted reproduction. As such, this case suggests that oocyte retrieval from transgender men who continue testosterone therapy throughout COS can be a viable and safe choice with proper obstetric support. This is important because the effects caused by the discontinuation of testosterone are damaging to transgender men's mental health.²

This case also emphasizes the need for further research on the topic since the patient's aneuploidy rate, ovarian reserve, and ovarian stimulation course length deviated from the average values. The expected aneuploidy rate for a 33-year-old cisgender woman is 31%.¹³ However, in this patient, 4 of 5 (80%) embryos harvested were aneuploid. This finding suggests that testosterone administration may increase the oocyte aneuploidy rate. Indeed, the role of high testosterone in pregnancy has been studied in the setting of cisgender women with polycystic ovary syndrome. Prior studies in that population suggest that an elevated testosterone level may increase recurrent miscarriage.¹⁵ However, other studies show that an elevated testosterone level has no impact on miscarriage.¹⁶ The discord among such studies highlights the need for continued investigation regarding elevated testosterone and its impact on aneuploidy and miscarriage.

Additionally, this patient had an above-average ovarian reserve. Increased ovarian reserve has been reported in cisgender women with polycystic ovary syndrome and has been attributed to androgen excess.¹⁷ Increased testosterone levels in transgender men may also contribute to an above-average ovarian follicle pool. Lastly, our patient underwent a 14-day course of COS, higher than the average (7–12 days).¹⁸ Given the high cost of fertility treatment, a longer necessary course could be a barrier to care for some patients.

Conclusion

More cases and further research are required to understand the effects of increased testosterone levels during assisted reproduction since all of the aforementioned observations could also be random variation from the mean due to the small sample size.

Ultimately, this case demonstrates that it may be feasible for transgender men to remain on testosterone during co-IVF: including successfully and safely undergoing oocyte retrieval with implantation into a cisgender female gestational carrier. However, the number of cytogenetically abnormal embryos harvested from

this patient suggests that testosterone has a deleterious effect on oocyte quality. Further studies investigating the effects of testosterone on assisted reproduction should be performed to provide transgender men with the best options for reproduction.

Disclosure

The authors have no multiplicity of interest to disclose.

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