Case Report

Spontaneous conception during in vitro fertilization prior to embryo transfer during the COVID-19 lockdown

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Abstract

Intercourse during IVF treatment traditionally had been discouraged for the purpose of avoiding trauma to the hyperstimulated ovaries, optimizing semen parameters, and preventing multifetal conception and ovarian hyperstimulation syndrome. The probability of spontaneous conception during an IVF cycle is minimal; however, a few cases have been reported in the literature. Recently, there was a case of unexplained infertility with no conception for 12 years and she conceived spontaneously post ovum pickup prior to embryo transfer. Previously she underwent six cycles of follicular monitoring timed intercourse and six cycles of IUI. Given the infrequent prevalence of such an occurrence, we aim to present and discuss this case.

Keywords: Fertilization, fertilization in vitro, infertility

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INTRODUCTION

Unexplained infertility is a condition when there are no obvious organic causes of infertility but the couple is unable to conceive after a year of regular intercourse. It is a diagnosis of exclusion. The incidence has been reported to be around 15% to 30%.[1] The diagnostic testing available identifies only the major reasons why a couple may have a difficult time getting pregnant. Normal couples generally have a 10% to 20% chance of conceiving each month, whereas couples suffering from unexplained infertility have only 1% to 4%.[2] Often the subtle infertility factors of unexplained infertility can be seen during IVF, so IVF can also be diagnostic. For example, if a woman has poor egg quality, it cannot be determined unless evaluated under a microscope during the procedure of IVF. Also, fertilization issues, implantation problems, genetic incompatibility between male and female partners, and embryo quality can be found out during an IVF cycle.[3,4]

Historically, the probability of spontaneous conception occurring during any given IVF cycle is very minimal.[5] By concept, IVF treatment for infertility is performed on patients with unexplained or explained infertility, when the chances of spontaneous conception are dismal. There are only two cases reported in the literature of spontaneous conception during an IVF cycle, and no such cases are reported in Nepal. This report presents a description of a very unique case where spontaneous conception occurred during IVF treatment in a patient with unexplained infertility for 12 years, prior to embryo transfer.

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CASE PRESENTATION

A 38-year-old nulliparous female presented to the clinic after trying to conceive for 12 years without success. Her cycle length varied from 26 to 28 days. Body mass index was 30. The previous workup showed normal hormone levels and a hysterosalpingogram. The antral follicle count was six.

The patient's partner had a normal semen analysis. The patient had previously undergone six cycles of letrozole and timed intercourse and eight cycles of intrauterine insemination, which were unsuccessful.

The decision was then made to move forward with IVF with embryo freezing, taking the patient's age into account. For her stimulation protocol, she began with 75 units of human menopausal gonadotropin and 50 mg clomiphene citrate for 5 days. The dose of HUMOG was subsequently increased to 225 mg sc from Day 6 and on Day 6 Inj Cetrolix 0.25 was also started. hCG trigger was administered on stimulation Day 10, at which point the patient was found to have six follicles of 20, 18, 17.5, 16.5, 16, 15, and 15 mm. Oocyte retrieval occurred 36 hours later where all follicles were aspirated, and six oocytes were obtained. Four eggs of the M2 quality were obtained and three embryos were formed of the quality 8I, 8I, 8II, all frozen on Day 3.

Though patients are usually instructed not to have intercourse during the IVF stimulation protocols, the patient had unprotected intercourse approximately 12 to 14 hours after hCG administration. The patient attributed this mistake to not understanding the verbal instructions given properly. Post ovum pickup, the patient was instructed to follow up at the clinic on the second day of her menses. As there was a lockdown due to the COVID-19 situation, the patient was lost to follow-up. The patient came to the clinic after 2 months when the lockdown situation eased with the complaint of not having her menses for 3 months post pickup. She had not done a home pregnancy test. Transvaginal ultrasound was done at the clinic that confirmed an intrauterine pregnancy with positive fetal cardiac activity consistent with 8 weeks 4-day gestation, suggesting conception around the time of oocyte retrieval. The couple gave a history of having intercourse 1 day after triggering (even though she was advised not to by the clinic) and 3 days post pickup as well. She advised to follow up for antenatal care, but she was again lost to follow up due to another lockdown. She was contacted on the phone and said that she was doing her antenatal checkup at a hospital nearby. She proceeded to have an elective cesarean section for breech presentation at 38 weeks 6 days period of gestation and delivered a healthy male newborn with weight of 3.2 kg.

DISCUSSION

The likelihood of pregnancy without treatment among couples with unexplained infertility is less than that of fertile couples. A retrospective review of 45 studies by Guzick *et al.* found an average cycle fecundity of 1.3% to 4.1% in the untreated groups, which was lower than most treatment interventions.[6] In a study on unexplained infertility, patients on a waiting list for IVF in the Netherlands had a 10% to 15% cumulative chance of pregnancy over a 12-month period.[7] Hence, many couples including the index patient opted for artificial reproduction due to the low chances of spontaneous conception.

An in vitro fertilization cycle involves ovarian stimulation with injectables, then retrieval of oocytes, and finally implantation back into the uterus. The most invasive procedure of these is considered to be the oocyte retrieval, the aim of which is to surgically retrieve all the oocytes from the ovaries. Most IVF practitioners have on occasion recovered additional oocytes from the cul-de-sac when they have suctioned the serosanguinous fluid at the end of the retrieval.[8] It is scientifically less likely to get oocyte post ovum pickup, given that most of them have been removed. However, it is possible that an oocyte that was missed inadvertently during the procedure or an oocyte that was lost in the peritoneal cavity led to this index pregnancy. We suspect this is the mechanism of pregnancy in the index scenario.

Intercourse is not recommended during peri-ovum pickup time given that unprotected intercourse can lead to spontaneous conception from sperm that could have survived in the female reproductive tract for several days.[9] Furthermore, sperm survival from intercourse may be prolonged in the presence of copious cervical mucus as seen with high levels of estrogen in stimulated cycles. Moreover, if conception does occur, there exists a possibility of multiple conceptions and possible ovarian hyperstimulation syndrome.[10]

A previous case report from 2001 described the first known incidence of simultaneous spontaneous and IVF conception, which resulted in a quadruplet pregnancy. In such a scenario, there is a risk for pregnancies at risk of complications such as preterm labor, preterm birth, preeclampsia, and placental abnormalities.[11]

Bavan and Milki in 2019 also reported a case of a patient undergoing IVF with the intention of the subsequent frozen embryo transfer after preimplantation genetic testing (PGT), but she conceived before the opportunity for embryo transfer.[9] Similar to our index case, the patient mentioned in this case had unprotected intercourse 6 days prior to egg retrieval. Bavan highlights that spontaneous conception during IVF compromises the ability to transfer embryos that are euploid, unaffected by single gene disorders, or intended for gender balancing within a family when desired. Owing to the COVID-19 situation, in the index case PGT was not done. Embryos were frozen until conditions would be favorable to resume fertility treatment.

Many difficulties faced in the management of the patients may be attributed to the confusion created by the COVID-19 pandemic. Owing to the lockdown, many patients were not able to follow up. The index patient may have landed up with life-threatening ovarian hyperstimulation syndrome. Clear guidelines were not given regarding how to manage the patients undergoing fertility treatment during the pandemic by the national fertility society in Nepal.

As fertility treatment was not considered an emergency medical service, it was a challenge to manage patients undergoing stimulation or ovum pickup and to follow up with the patients who had just undergone the procedure. Many patients like the index patient said they were stopped on the way to the clinic as their condition was not an "emergency." Although the index patient had a favorable outcome, there were high chances of the patient landing up with multifetal gestation and possible ovarian hyperstimulation syndrome. Fertility services were rather neglected when health-related policies were being made in Nepal during the COVID-19 pandemic and most fertility clinics had to look toward Western Countries and their guidelines as an example.

CONCLUSION

A spontaneous conception in a woman post ovum pickup prior to embryo transfer occurred that led to a successful singleton pregnancy. Although the outcome turned out favorably for the index patient, intercourse peri-oocyte retrieval time may be associated with multiple pregnancies and life-threatening complications such as ovarian hyperstimulation syndrome and hence should still be discouraged. The COVID-19 pandemic generates a big challenge to the management and continuous monitoring of infertility treatment and adequate fertility guidelines need to be established during the pandemic.

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Conflicts of interest

There are no conflicts of interest.

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