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Should sexual intercourse be avoided during the embryo transfer cycle? Life-threatening ruptured heterotopic pregnancy after single thawed embryo transfer: case report and review of the literature

Y. Aoki, J. Kumakiri, A. Itakura, I. Kikuchi, N. Takahashi, T. Satoru

Department of Obstetrics and Gynecology, Juntendo University School of Medicine, Tokyo (Japan)

Summary

Background: To report the life-threatening complication of a raptured heterotopic pregnancy occurring from thawed single embryo transfer. *Case Report:* A 33-year-old woman underwent in vitro fertilization (IVF) under a step-up regimen. After oocyte collection, blastocysts were frozen, and a single frozen-thawed blastocyst was then transferred according to the natural cycle. On day 17 after embryo transfer, an intrauterine pregnancy was confirmed. On day 28, she complained of sudden abdominal pain and ultrasonography revealed marked fluid retention in the peritoneal cavity. Emergency laparoscopy was performed, revealing hemoperitoneum and a ruptured interstitial heterotopic pregnancy (HP), which was then resected laparoscopically. Because sexual intercourse had occurred shortly before the transfer, a HP comprising a spontaneous pregnancy and a pregnancy achieved by assisted reproductive technology was assumed. The fetus in the uterus survived and was delivered. *Conclusion:* In this case, however, despite the single embryo transfer during the natural-cycle frozen-thawed embryo transfer process, the risk of life-threatening complication as a HP as a consequence of spontaneous pregnancy after sexual intercourse remained.

Key words: Heterotopic pregnancy; Single embryo transfer; Laparoscopy; Interstitial pregnancy; Hemoperitoneum.

Introduction

Heterotopic pregnancy (HP) is a rare disorder with an incidence of approximately 1/30,000 spontaneous pregnancies [1]. However, the incidence has recently increased to 1/100 pregnancies with the use of ovulation inducing agents [2].

The present authors encountered an HP in a patient who, three years previously, had undergone left salpingectomy. A uterine pregnancy was confirmed after frozen-thawed single blastocyst transfer. The subsequent occurrence of acute hemoperitoneum led to laparoscopic detection of a ruptured pregnancy in interstitial segment of the resected fallopian tube, and the ruptured pregnancy was laparoscopically resected. The intrauterine pregnancy continued after surgery, and a live cesarean birth followed.

Case Report

The present patient provided informed consent for the operative procedures to be video-recorded and photographed and for the clinical data to be used for research purposes, with the understanding that the information would be anonymized.

The patient was a 33-year-old woman, gravida 2, para 0. She had undergone laparoscopic left salpingectomy for a left tubal pregnancy, and she experienced a spontaneous abortion. She was taking oral levothyroxine sodium hydrate for hyperthyroidism.

In spite of timed intercourse therapy for nine months, pregnancy was not achieved. Therefore the treatment strategy was changed to in vitro fertilization (IVF) with a step-up regimen. The patient was given clomiphene citrate orally at 100 mg/day for five days starting on day 3 of the menstrual cycle, and human menopausal gonadotropin was intramuscularly injected at 150 IU on the fifth, seventh, and ninth days of the menstrual cycle. On day 11 of the menstrual cycle, the dominant ovarian follicle reached 18 mm in diameter. Human chorionic gonadotropin 5,000 IU were injected intramuscularly to promote oocyte maturation, and ooctyes were retrieved 35 hours later. Conventional IVF was carried out, and one three-day-old embryo consisting of eight cells in G1 phase (Veeck classification) was frozen by the Cryotop method [3]. For the remaining embryos, the medium was changed to Sydney IVF blastocyst medium. 4BB (Gardner classification) blastocyst were frozen by the Cryotop method.

The first thawed single embryo transfer (SET) had failed. After two additional menstrual cycles had passed, ovulation was confirmed on day 13 of the natural menstrual cycle. Six days after ovulation, a spontaneously hatching grade 5BB blastocyst was thawed and transferred. For luteal phase support, 30 mg/day dydrogesterone was started on the day after ovulation was con-

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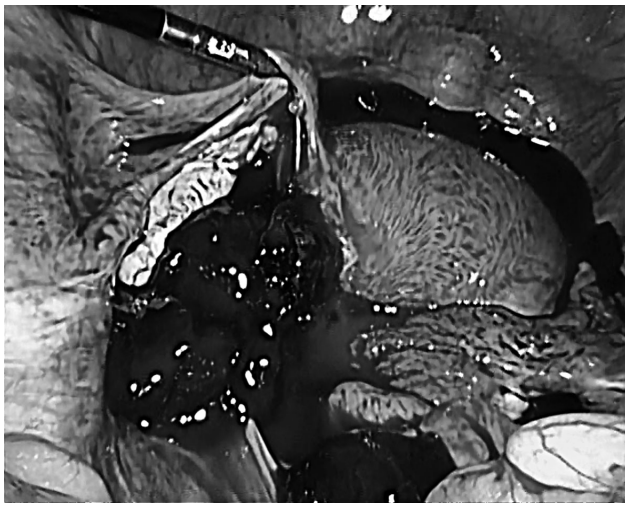

Figure 1. — Laparoscopic view of the peritoneal cavity showing the presence of blood.

firmed. On day 10 after the SET, the patient's blood beta-human chorionic gonadotropin level was 375.5 mlU/ml, indicating an established pregnancy. On day 24, a fetal heart beat was detected in the uterus.

On day 28 after SET, the patient visited the present hospital complaining of lower abdominal pain. Transvaginal ultrasonography revealed marked fluid retention in the peritoneal cavity. Emergency laparoscopy was performed the same day, revealing hemoperitoneum and a ruptured interstitial HP, which was then resected laparoscopically. The authors found that 750 ml of blood had accumulated in the peritoneal cavity (Figure 1). In the interstitial segment of the left fallopian tube (which remained after salpingectomy), a mass was detected and then extirpated by wedge resection. The interstitial portion of the uterus at the resection margin was closed by double-layer continuous suturing with absorbable thread. Postoperative transabdominal ultrasonography confirmed a fetal heart beat in the uterus.

During a postoperative interview, the patient revealed that she had had sexual intercourse (SI) around day 13 of the menstrual cycle. On the basis of the surgical findings and the clinical course, simultaneous establishment of a pregnancy with the transferred embryo and a spontaneous pregnancy were assumed. The pathology examination revealed villi and trophoblastic cell components. The diagnosis was a ruptured left interstitial tubal component of an HP.

The intrauterine pregnancy continued without major complications. At 36 weeks and two days of gestation, uterine contractions began, so elective cesarean section was performed to avoid rupture of uterus that could have occurred during normal delivery. A healthy female neonate weighing 2,518 grams was delivered.

Discussion

SET is a procedure used in assisted reproduction to avoid a multiple pregnancy with complications [4]. To determine the frequency of HP resulting from SET, using "heterotopic pregnancy" and "single embryo transfer" as keywords, the authors searched the PubMed database for articles published between 1978 and 2015, and they found five English-language reports [5-9]. However, only one report described HP after SET. They also found four reports (five cases) [10-13] of a dizygotic twin pregnancy occurring after SET. These were recognized as such because the babies' sex differed. Four of the patients reported having SI during the transplantation cycle, so it is possible that these patients became pregnant naturally as well as by SET.

IVF embryo transfer is performed to make pregnancy possible. Nevertheless, opinions vary from institution to institution whether SI should be allowed during the transplant period. There is a reported case in which the combination of SET and SI resulted in a twin pregnancy [10]. It can be argued that SI improves the outcomes of ART [14]. The present authors cannot ignore the possibility that SI during the transfer cycle facilitated embryo implantation in this case.

Gergolet *et al.* [9] emphasize the risk of SI around the time of SET. It was quite clear in their case that one of the pregnancies was the result of SI that occurred at the time of controlled ovarian hyperstimulation. This situation is quite different from the present case, which resulted from frozen-thawed SET during the natural menstrual cycle. On the basis of the present experience and research, the authors believe that it is best to avoid SI during the transplantation cycle also. The authors can only make assumptions about the genetic relationship between the two HP components in this case because they did not perform a twin zygosity DNA test on the extracted fallopian pregnancy.

Conclusion

SET is a procedure used to avoid multiple pregnancy with its potential complications. However, even in cases of frozen thawed SET, when no restriction is placed on SI, we should be aware of the possibility of serious life-threatening complications such as HP.

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References

[1] Reece E.A., Petrie R.H., Sirmans M.F., Finster M., Todd W.D.: "Combined intrauterine and extrauterine gestations: a review". *Am. J. Obstet. Gynecol*.,1983, *146*, 323.

[2] Tal J., Haddad S., Gordon N., Timor-Tritsch I.: "Heterotopic pregnancy after ovulation induction and assisted reproductive technologies: a literature review from 1971 to 1993". *Fertil. Steril*., 1996, *66*, 1.

[3] Kuwayama M., Vajta G., Kato O., Leibo S.: "Highly efficient vitrification method for cryopreservation of human oocytes". *Reprod. Biomed. Online,* 2005, *11*, 300.

[4] Roberts S.A., McGowan L., Mark Hirst W., Vail A., Rutherford A., Lieberman B.A., *et al.*: "Reducing the incidence of twins from IVF treatments: predictive modelling from a retrospective cohort". *Hum Reprod*., 2011, *26*, 569.

[5] Mancini F., Clua E., Martínez F., Battaglia C., Veiga A., Barri P.N.: "Heterotopic pregnancy in a cross border oocyte donation patient: the importance of cooperation between centers". *Fertil. Steril*., 2011, *95*, 2432.e13.
[6] Lautmann K., Staboulidou I., Wüstemann M., Günter H., Scharf A., Hillemanns P.: "Heterotopic pregnancy: simultaneous intrauterine and ectopic pregnancy following IVF treatment with the birth of a healthy child". *Ultraschall. Med*., 2009, *30*, 71.
[7] Ludwig M., Riethmüller-Winzen H., Felberbaum R.E., Olivennes F., Albano C., Devroey P., *et al.*: "Health of 227 children born after controlled ovarian stimulation for in vitro fertilization using the luteinizing hormone-releasing hormone antagonist cetrorelix". *Fertil. Steril*., 2001, *75*, 18.
[8] Johnson N., McComb P., Gudex G.: "Heterotopic pregnancy complicating in vitro fertilization". *Aust. N. Z. J. Obstet. Gynaecol*., 1998, *38*, 151.
[9] Gergolet M., Klanjscek J., Steblovnik L., Teran N., Bizjak N., Di Bon N., *et al.*: "A case of avoidable heterotopic pregnancy after single embryo transfer". *Reprod. Biomed. Online*, 2015, *30*, 622.
[10] Van der Hoorn M.L., Helmerhorst F., Claas F., Scherjon S.: "Dizygotic twin pregnancy after transfer of one embryo". *Fertil. Steril*., 2011, *95*, 805e1.
[11] Kyono K., Nakajo Y., Nishinaka C., Araki Y., Doshida M., Toya M., *et al.*: "A birth of twins—one boy and one girl—from a single embryo transfer and a possible natural pregnancy". *J. Assist. Reprod. Genet*., 2009, *26*, 553.
[12] Sugawara N., Fukuchi H., Maeda M., Komaba R., Araki Y.: "Sex discordant twins despite single embryo transfer: a report of two cases". *Reprod. Med. Biol*., 2010, *9*, 169.
[13] Takehara I., Takahashi T., Hara S., Matsuo K., Igarashi H., Kurachi H.: "Dizygotic twin pregnancy after single embryo transfer: a case report and review of the literature". *J. Assist. Reprod. Genet*., 2014, *31*, 443.
[14] Tremellen K.P., Valbuena D., Landeras J., Ballesteros A., Martinez J., Mendoza S., *et al.*: "The effect of intercourse on pregnancy rates during assisted human reproduction". *Hum. Reprod*., 2000, *15*, 2653.

Corresponding Author:
Y. AOKI, M.D.
Department of Obstetrics and Gynecology
Juntendo University School of Medicine
Hongo 2-1-1, Bunkyo-ku
Tokyo 113-8421 (Japan)
e-mail: youichiaokijp@yahoo.co.jp