

SIMULTANEOUS BILATERAL TUBAL PREGNANCY AFTER *IN VITRO* FERTILIZATION AND EMBRYO TRANSFER

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SUMMARY

Objective: Ectopic pregnancies are known to occur with increased frequency after *in vitro* fertilization (IVF) and related techniques. We present a case of bilateral tubal pregnancy following IVF and embryo transfer (ET).

Case Report: A 27-year-old woman was referred to our IVF clinic because of primary infertility, and underwent three cycles of IVF-intracytoplasmic sperm injection treatment. In her third cycle, 32 days after ET, she suffered from pelvic pain and vaginal bleeding. Transvaginal ultrasonography revealed bilateral tubal ectopic pregnancy with fluid in the pouch of Douglas but no intrauterine gestational sac. One of the embryos had fetal heart motion. Laparoscopic bilateral salpingostomy was performed immediately. The postoperative course was uneventful. Pathologic examination also identified chorionic villi and placental tissue in both tubes, and an Arias-Stella reaction without villi in the endometrium.

Conclusion: The diagnosis of ectopic or heterotopic pregnancy should always be considered in patients undergoing IVF-ET because of its increased incidence with this technique compared with natural conception. Although the incidence of bilateral tubal pregnancy is not high, sonographers and surgeons should examine both adnexa when diagnosing an ectopic pregnancy, especially in IVF-ET patients. Early diagnosis is essential for the prevention of significant maternal morbidity and mortality. [*Taiwan J Obstet Gynecol* 2008;47(3):338-340]

Key Words: bilateral tubal pregnancy, IVF-ET

Introduction

Ectopic pregnancies are known to occur with increased frequency after *in vitro* fertilization (IVF) and related techniques. Several theories have been put forward to account for the occurrence of ectopic implantation after transcervical uterine embryo transfer (ET). Potential factors include the possibility of direct injection of embryos into the fallopian tube, uterine contractions provoked by the transfer catheter in the uterine cavity, and the volume of transfer medium [1]. Steptoe and Edwards reported the first case of IVF resulting in an ectopic

pregnancy [2]. The high incidence of ectopic pregnancy associated with IVF-ET continues to be a problem, but simultaneous bilateral tubal pregnancy following IVF-ET is a rare condition.

We present the case of a 27-year-old IVF patient with simultaneous bilateral tubal pregnancy and no intrauterine pregnancy after transfer of three embryos.

Case Report

The patient was a 27-year-old woman with a 6-year history of primary infertility. She had been treated by ovulation induction and artificial insemination with her husband's sperm three times but failed to conceive. Prior to her referral to our IVF clinic, hysterosalpingography revealed patent tubes and an adequate uterine cavity. Her basal hormone profile was normal and



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transvaginal ultrasonography (TVUSG) revealed bilateral polycystic ovaries and normal uterus on the third day of the menstrual cycle. Her husband's semen analysis showed oligospermia (sperm count, $8 \times 10^6/\text{mL}$; motility, 25%; normal morphology, 1%).

The patient underwent two IVF cycles and failed to conceive. In her third IVF-ET cycle, she received the long protocol of gonadotropin-releasing hormone (GnRH) agonists from the previous mid-luteal phase followed by recombinant follicle-stimulating hormone and human menopausal gonadotropin from day 3 of the menstrual cycle. Follicular development was monitored by plasma estradiol (E_2) and follicular diameter by TVUSG from day 6. On day 12 of the cycle, when the plasma E_2 level was 1,896 pg/mL, 10,000 IU of human chorionic gonadotropin (hCG) was administered intramuscularly. Transvaginal oocyte retrieval was performed 36 hours later under sonographic control, yielding seven oocytes. Intracytoplasmic sperm injection was performed and three D3 embryos were transferred transcervically using a Wallace catheter. The luteal phase was supported with hCG. Thirty-two days after ET, she was referred to our clinic, suffering from pelvic pain and vaginal bleeding. TVUSG revealed an ectopic ring 30×16 mm in diameter containing an embryo with a crown-rump length of 4 mm and fetal heart motion in the right fallopian tube, and a second ectopic ring 28×17 mm in the left tube. Bilateral ovaries were 4–5 cm in diameter. β -hCG level was 3,091 IU/L. Laparoscopy was performed and confirmed the diagnosis of bilateral tubal pregnancy. Both of the ectopic pregnancies were unruptured and located at the isthmic-ampullary portion of the fallopian tubes. Bilateral salpingostomy and probe curettage were performed. The patient had an uneventful recovery. Pathologic examination identified chorionic villi and placental tissue in both tubes, concordant with bilateral tubal ectopic pregnancy. Probe curettage of the endometrium revealed an Arias-Stella reaction and decidua without villi.

Discussion

Several risk factors are associated with ectopic pregnancy, including tubal factors (salpingitis, tubal surgery, sterilization, previous ectopic pregnancy), zygote abnormalities, ovarian factors and exogenous hormones and pelvic adhesions [3]. Tubal ectopic pregnancy after IVF-ET is being recognized with increasing frequency, but simultaneous bilateral tubal pregnancies have been reported on only a few occasions.

The increased risk of tubal ectopic pregnancy associated with IVF-ET has been confirmed in many studies

[4,5]. Marcus and Brinsden reported six bilateral tubal pregnancies among 135 ectopic pregnancies after IVF-ET [4]. The techniques of embryo and gamete transfer, number and quality of embryos and gametes replaced, pelvic and tubal condition, hormonal milieu, and superfecundations are well-known risk factors [6]. Excessive medium and improper catheter insertion may lead to dispersion of embryos, called the "spray and drift" effect [6,7]. The volume of culture medium transferred is thought to be one of the factors related to ectopic pregnancy in IVF-ET [4]. Lee et al recommend that the volume of transferred medium should not exceed 20 μL [8]. It also seems reasonable to conclude that whatever the mechanism involved, the risk will be greater if more embryos are transferred. In the few reports describing bilateral ectopic pregnancies following IVF-ET, more than two embryos were transferred [9]. In addition, abnormal hormonal secretion and/or exogenous hormones may play a role in ectopic gestation. This may be due to progesterone's smooth muscle relaxant effects [3]. There are also several reports in the literature suggesting that GnRH analog use may be linked to a higher rate of ectopic pregnancy in the IVF population [7].

The most important technique for the diagnosis of ectopic pregnancy is high-resolution TVUSG. Generally, if the serum β -hCG level is $> 1,500$ – $2,000$ IU/L without a gestational sac detectable in the uterus by TVUSG, the patient is regarded as having an ectopic pregnancy. The absence of an intrauterine pregnancy with a raised hCG level is consistent with an abnormal pregnancy, but does not distinguish a miscarriage from an ectopic pregnancy. When the initial hCG value is low, serial hCG values can be used to determine whether a gestation is potentially viable or spontaneously resolving. The minimal rise in hCG for a viable pregnancy is 53% in 2 days. The minimal decline in a spontaneous abortion is 21–35% in 2 days, depending on the initial level. A rise or fall in serial hCG values that is slower than this, is suggestive of an ectopic pregnancy [10]. Ninety point nine percent of ectopic pregnancies can be accurately diagnosed using TVUSG prior to surgery [11]. In our patient, sonographic diagnosis was confirmed by laparoscopy and histopathology.

This patient had no history of pelvic operation or previous ectopic pregnancy. A high E_2 level (1,896 pg/mL) on the day of hCG injection and luteal phase support by hCG may be considered as risk factors. Three embryos were transferred, with no difficulty experienced in inserting the Wallace catheter into the cavity, and an appropriate amount of culture medium (15 μL) was transferred. The most likely cause of the bilateral ectopic pregnancy in this case was thought to be the "spray effect".

In terms of the surgical treatment of ectopic pregnancy, the benefits of salpingectomy over salpingostomy are uncertain [12]. In women of reproductive age with tubal pregnancies, salpingostomy is the preferred method. However, salpingectomy is a better treatment for women with severely damaged fallopian tubes, recurrent ectopic pregnancies in the same tube, uncontrolled bleeding after salpingostomy, large tubal pregnancies (> 5 cm), heterotopic pregnancies, and for those who have completed their families [13]. In the present case, following sonographic diagnosis, bilateral salpingostomy was performed because neither of the tubes were severely damaged and the pregnancies were < 5 cm. Unfortunately, bilateral salpingectomy cannot totally prevent subsequent heterotopic pregnancies [14].

Because women who undergo IVF programs are at increased risk of ectopic pregnancies, screening with repeated TVUSG and hCG assays is mandatory. Although the incidence of bilateral tubal pregnancy is not high, both sonographers and surgeons should examine both adnexa when diagnosing an ectopic pregnancy, especially in an IVF patient.

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