Tubal Pregnancy Following Tubal Embryo Transfer into the Contralateral Fallopian Tube

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Ectopic and heterotopic pregnancy may occur with increased frequency following assisted reproductive technology (ART) procedures. In addition, there may be unusual sites of implantation, which may cause atypical and confusing clinical manifestations. We present a case of tubal pregnancy after tubal embryo transfer (TET) to the contralateral fallopian tube. Four embryos were transferred to the left fallopian tube by laparoscopy, but the patient developed a right tubal pregnancy, possibly as a result of intrauterine or intra-abdominal migration of the embryo. ART patients must be followed closely soon after the procedure, and there should be a high index of suspicion for an unusual implantation site.

KEY WORDS: Ectopic pregnancy; in vitro fertilization; tubal embryo transfer.

INTRODUCTION

The first human pregnancy reported after in vitro fertilization (IVF) and embryo transfer (ET) was ectopic (1). Approximately 5% of clinical pregnancies after IVF are ectopic (2–4). This is an important issue in assisted reproductive technology (ART), not only because it usually means failure of the procedure to achieve a normal intrauterine pregnancy, but also because it is a life-threatening emergency. It has been suggested that the incidence of ectopic pregnancy may be increased following ART procedures, particularly with unusual sites of implantation (5), which may cause atypical and confusing clinical manifestations. We present a case of tubal pregnancy after tubal embryo transfer (TET) to the contralateral fallopian tube.

CASE REPORT

The patient was a 37-year-old woman, gravida 0, with a 6-year history of primary infertility. Her husband's semen analysis was normal. She had patent fallopian tubes bilaterally and a normal uterine cavity on hysterosalpingography. On pelvic examination, she had a retroflexed uterus with the size of a goose egg and tender nodules in the cul-de-sac. The impression was primary infertility due to endometriosis, and therapeutic options were discussed with the patient and her husband. The decision was to proceed with IVF and TET.

Subcutaneous injection of leuprolide acetate (Lupron; Abbott Laboratories, Illinois) 0.1 cc per day for pituitary desensitization was started on November 28, 2002, the 18th day of the patient's previous menstrual cycle. Gonadotropins were given from day 3 of menstruation, with 2 ampoules of human menopausal gonadotropin (HMG, Pergonal; Serono, Rome, Italy) and 2 ampoules of recombinant follicle stimulating hormone (rFSH, Gonad-F; Serono, Aubonne, Switzerland). When three leading follicles reached a mean diameter of 18 mm, 10,000 IU of human chorionic gonadotropin (HCG, Pregnyl;

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Organon, Oss, The Netherlands) were given on day 15 of the menstrual cycle. Transvaginal ovum pick up (OPU) was carried out under sonographic guidance 36 h later. The estradiol level on the day of HCG injection was 1778 pg/dL. Six mature oocytes were recovered from the right ovary and one from the left. All six underwent successful fertilization after insemination.

Two days after OPU, the patient underwent laparoscopy for TET. A GIFT catheter (k-GIFT-1010, Cook, Queensland, Australia) was used to transfer four embryos in 20 μ L of G1.2 medium (Vitrolife; Goteborg, Germany). The embryos were at the four-cell stage and of good quality. An enlarged right ovary obscured a view of the right fallopian tube, so all four embryos were transferred into the left tube, with the transfer bolus deposited 3 cm from the fimbria. The entire process was continuously monitored laparoscopically and was atraumatic. Following TET, the patient remained supine for 4 h and then was discharged.

Luteal phase support was provided with 2500 IU of HCG on day 2 and day 5 after OPU, and micronized progesterone (Utrogestan, Laboratoires Piette International S.A.; Brussels, Belgium) at a dose of 600 mg/day commencing on the next day after OPU. On day 18 after OPU, the urine pregnancy test was positive. However, the patient experienced vaginal spotting beginning day 21 after OPU. Transvaginal sonography on day 31 revealed a thick endometrium of 35 mm but no visible intrauterine pregnancy. Although a 5.4 $\times$ 4.7 cm right adnexal mass was found by sonography, it was assumed to be the right ovary, persistently enlarged after controlled ovarian hyperstimulation (COH). Our initial impression was incomplete abortion.

The patient underwent dilatation and curettage on day 32 after OPU. However, pathologic examination revealed only decidualized endometrial tissue with an Arias-Sella reaction. No chorionic villi or trophoblasts were identified. Her serum β -HCG was 4487 IU/L, and a 5-cm right adnexal mass was seen on transvaginal sonography, strongly suggestive of a right tubal pregnancy. Laparoscopy was performed on day 38 after OPU, revealing a hemoperitoneum with about 500 mL of blood and a right hematosalpinx. Right salpingectomy was performed and a tubal pregnancy was confirmed histopathologically.

The postoperative course was uneventful and the patient was discharged the next day. She is now

awaiting thawing and transfer of her cryopreserved embryos.

DISCUSSION

Ectopic pregnancy is a life-threatening gynecologic emergency in which there has been successful fertilization but incorrect implantation. In the IVF program in our hospital from 1998 to 2001, there were 345 clinical pregnancies, of which 9 (2.6%) were ectopic. More than 95% of ectopic pregnancies occur in the fallopian tubes. Rarely, embryos implant in the pelvic cavity, causing ovarian or abdominal pregnancies. To our knowledge, there is no previously published report of tubal pregnancy after TET into the contralateral fallopian tube such as our patient had.

Verhulst *et al.* (6) reported that the incidence of ectopic pregnancy was not influenced by the number of replaced embryos or the transfer route, e.g., intrauterine or intrafallopian transfer. Other authors have concluded that tubal pathology is the major risk factor (6–8). However, patients considered for TET in our hospital are considered to have relatively normal fallopian tubes by hysterosalpingographic or laparoscopic evaluation, although subclinical tubal disease cannot be ruled out in our patients.

The curious fact in this case is that the ectopic implantation occurred in the tube of the contralateral side, rather than the tube in which the embryos were placed. There are two routes the embryo might have taken to get to the other side, either intrauterine or intra-abdominal.

In the first scenario, the embryo would have to exit the left tube into the uterine cavity and then move upstream into the lumen of the right fallopian tube. Several groups have advanced this explanation for ectopic pregnancy after IVF with intrauterine ET. It has been suggested that deep fundal ET (9,10) or use of a large volume of transfer medium (3,7) might place the embryos near the orifice of a fallopian tube and increase the risk of tubal ectopic pregnancy. We used only 20 μ L of transfer medium and continuously monitored the TET procedure laparoscopically to make sure the embryos were deposited into the ampullar portion of the fallopian tube. Lesny maintained that the manipulation involved in ET might stimulate abnormal contractions in the uterine junctional zone (4,11). Fernandez *et al.* suggested that aberrant

hormonal environment induced by COH might induce abnormal cilia movement or peristalsis of the fallopian tubes (12,13). However, this mechanism could hardly explain why an embryo moving toward the uterine cavity from the left tube in a forward direction would then begin migrating in a retrograde direction into the right tube.

The more likely mechanism might be that an embryo moved out of the left tube into the pelvic cavity and was then captured by the fimbria of the right fallopian tube. There have been case reports of pregnancy in a noncommunicating rudimentary horn in patients with a unicornuate uterus, with an estimated incidence of 1 in 100,000 to 140,000 deliveries (14–16). In these cases, the fertilizing sperm had to migrate out of the fallopian tube on the patent side and cross transperitoneally to the contralateral, noncommunicating tube. Walters *et al.* reported that 16% of tubal ectopic pregnancies result from a contralateral ovulation (17). Sopelak and Bates (18) also documented the possibility of spontaneous conception in patients with only one tube but who had ovulated from the contralateral ovary. Transmigration of oocytes in the peritoneal cavity probably occurs infrequently, with the ovum usually picked up only with the fallopian tubes and ovaries situated close together in the cul-de-sac (19). The issue of an embryo, however, surviving in the pelvic environment so as to cross from one tube to the other is a different matter. There have been several case reports of ovarian or abdominal ectopic pregnancy after IVF/ET (20–25). We have had a case of abdominal pregnancy in the pelvic cavity after TET (unpublished data). Of particular note, Marcus and Brinsden (21) reported three cases of ovarian pregnancy on the side without a patent fallopian tube, demonstrating the possibility of intra-abdominal migration of embryos from the contralateral patent tube. Thus, it is possible that in our case, the embryo not only migrated transabdominally, but was then picked up by the contralateral fallopian tube.

A final possibility that should be considered is that there was in vivo fertilization of unrecovered oocytes from the right ovary, if there had been coitus near the time of OPU (26). We routinely advise patients in our IVF program not to have sexual intercourse and therefore consider this possibility to be very unlikely.

In summary, we have presented here an unusual case of tubal pregnancy following TET to the contralateral fallopian tube. Since ectopic and heterotopic pregnancies are more common with ART than

after spontaneous conception, it is imperative to follow patients closely once pregnancy is established to verify the site of implantation. The possibility of implantation in the contralateral tube after TET cannot be discounted.

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