SHORT COMMUNICATIONS

NEW YORK, NEW YORK

Combined Intrauterine, Tubal, and Cervical Pregnancies Following In Vitro Fertilization and Embryo Transfer

Submitted: February 20, 2001

Accepted: March 7, 2001

INTRODUCTION

Combined intrauterine and extrauterine pregnancy (heterotopic pregnancy) has an incidence of 1 in 4,000–30,000 pregnancies (1). Following in vitro fertilization (IVF) and embryo transfer (ET), the incidence is higher occurring in 1 in 2,600–8,000 pregnancies (2,3).

Cervical pregnancy occurs in 1 in 1,000–95,000 pregnancies, but accounts for 0.1% of IVF pregnancies and 3.7% of IVF ectopic pregnancies (4,5). Tubal ectopic pregnancy following IVF–ET has an incidence of 1.8–13.2% (5,6). A medline search from 1975 to December, 1999, using the key words, cervical pregnancy, heterotopic pregnancy, and IVF–ET, revealed no case of simultaneous pregnancies in the uterus, tube, and cervix following IVF–ET. We report the first case of combined intrauterine, tubal, and cervical pregnancies, and discuss their management and possible contributing factors.

CASE REPORT

A 33-year-old gravida 1, para 0-0-1-0 was referred for IVF–ET. Medical, surgical, and gynecologic histories were unremarkable. Prior infertility work-up revealed an intrauterine cavity defect noted on hysterosalpingogram for which the patient underwent hysteroscopic polypectomy, followed by ovulation induction using clomiphene citrate and intrauterine

insemination. She conceived following her first treatment cycle, but spontaneously aborted and underwent D&C without complications.

She elected to proceed with IVF, and received a standard protocol of leuprolide acetate pituitary suppression followed with twice daily dosing of three ampules of human gonadotropins for controlled ovarian hyperstimulation. Following administration of hCG and transvaginal ultrasound guided follicle aspiration with subsequent fertilization, 4 eight-cell embryos were transferred transcervically under ultrasound guidance. The patient received 90 mg of intravaginal Crinone 8%® (Columbia Research Laboratories, Paris, France) daily for luteal phase support starting on the evening of ET. Serum beta-hCG rose from 19 mIU/mL on Day 9 after ET, to 624 mIU/mL on Day 16 after ET.

On Day 24 after ET, the patient reported mild painless vaginal spotting, and transvaginal sonogram revealed three gestational sacs (intrauterine, tubal at the fimbriated end, and cervical at the level of the internal os) with systolic and diastolic blood flows confirmed by color Doppler ultrasound. The intrauterine sac had a fetal pole (CRL, 2 mm) and yolk sac, whereas the tubal and cervical pregnancies were both anembryonic. There was a small amount of free fluid in the posterior cul-de-sac. The woman was hemodynamically stable with a hematocrit of 37% and elected expectant management. As reported by daily telephone contact, she continued to have scant, painless vaginal bleeding without pelvic or abdominal pain. Beta-hCG increased to 17,428 mIU/mL on Day 26, while the hematocrit dropped to 33.8%. Continued growth of the intrauterine gestation (CRL, 2.6 mm) was demonstrated, with cardiac activity and a developing subchorionic hematoma (Fig. 1). The echogenic structure within the right tubal fimbria remained anembryonic and unchanged in size. The cul-de-sac fluid did not increase. The cervical gestation now had two embryonic poles (CRL, 4 mm). On Day 31 after ET, fetal heart activity was noted in both the cervical pregnancies and intrauterine pregnancy

Fig. 1. Transvaginal sonography, Day 31. (a) Sagittal midline view (from left to right) of intrauterine pregnancy with yolk sac, subchorionic hematoma, and cervical pregnancy. (b) Sagittal view of cervical pregnancy with 0.4-cm fetal pole. (c) Oblique view of cervical gestational sac with two fetal poles (arrows). (d) Transverse view of large right subchorionic hematoma and IUP with yolk sac.

(CRL, 5 mm) (Fig. 1), whereas the tubal pregnancy was completely resolved. However, the subchorionic hematoma measured $62 \times 32 \times 34 \text{ mm}^3$.

Options for intervention were rediscussed including surgical termination, medical termination with systemic and intraamniotic injection of methotrexate, or selective potassium chloride (KCL) puncture with reduction of the cervical pregnancy. The patient and her husband desired conservative management with the hope of saving the intrauterine pregnancy. On Day 37, although there was peripheral blood flow, no cardiac activity was detected in either the intrauterine or cervical gestational sacs and the subchorionic hematoma now measured $72 \times 35 \times 54 \text{ mm}^3$. Intramuscular methotrexate, 50 mg (1 mg/kg), was administered on Day 38 and again on Day 40 post-ET, following a rise in serum beta-hCG from 65,867 mIU/mL to 85,684 mIU/mL, and a small increase in blood flow around the periphery

of the cervical gestational sac. On Day 43, with reduced blood flow around the collapsed cervical gestational sac, D&C was performed under conscious sedation and ultrasound guidance with minimal blood loss. Weekly serum hCG levels were performed over the next 4 weeks until complete resolution was documented.

DISCUSSION

The occurrence of a cervical pregnancy in conjunction with a viable intrauterine pregnancy is rare. Monteagudo *et al.* described a case of successful transvaginal ultrasound-guided intraamniotic KCL injection of a cervical pregnancy with preservation of an intrauterine pregnancy delivered by cesarean at 34 weeks. Subsequently, the patient was treated with intramuscular methotrexate with prolonged resolution of the cervical pregnancy (7). To our knowledge, a

combined intrauterine, cervical, and tubal pregnancy has not been reported.

In the present case, as the woman wished to maintain the intrauterine pregnancy, counseling and management was difficult. She was given three options: 1) laparoscopic surgery to remove the tubal pregnancy and KCL injection of the cervical gestation; 2) KCL injection of both the tubal and cervical pregnancies; 3) termination of the pregnancy. Following laparoscopic salpingectomy or salpingostomy, maintenance of viability of a coexistent intrauterine gestation has been reported to be 60% (8). However, spontaneous resolution of the tubal pregnancy obviated the need for laparoscopy in our patient. The woman was counseled regarding the possible protracted course of cervical pregnancies treated by KCL puncture. They can increase in size and vascularity, behave like a placenta accreta, require hospitalization, and might require adjuvant methotrexate to hasten the resorption process (7). Methotrexate use has also been shown to decrease the risk of hemorrhage during curettage (9). When both intrauterine and cervical viability ceased, the woman was successfully treated with parenteral methotrexate followed by curettage under sonographic guidance.

Prior surgical uterine manipulation may predispose to cervical pregnancy (10), whereas a history of tubal infertility predisposes to tubal pregnancy (11). Our patient did have a history of hysteroscopic uterine polypectomy and D&C for pregnancy termination; however, no evidence of tubal infertility was found. Furthermore, avoiding the use of excessive volume of transfer medium (12), as well as midcavity placement of the catheter (13) have been associated with a lower rate of higher order ectopic pregnancies during ET. The volume of transfer medium used in our patient was less than 20 μ L. However, catheter placement was only 0.5 cm from the top of the uterine fundus, which may have led to the tubal pregnancy.

In conclusion, heterotopic pregnancies are rare, but are increased following cervical manipulation and/or assisted reproduction. Management is challenging, but early diagnosis allows for a planned and coordinated approach enabling various treatment modalities depending on the clinical circumstances.

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