UNILATERAL TWIN TUBAL PREGNANCY AND SUBSEQUENT HETEROTOPIC PREGNANCY IN A PATIENT FOLLOWING *IN VITRO* FERTILIZATION

Miro Kasum

University Department of Gynecology and Obstetrics, Zagreb University Hospital Center, Zagreb, Croatia

SUMMARY – Unilateral twin tubal gestations are extremely rare with a reported incidence of 1 *per* 200 ectopic pregnancies. In recent years, the incidence of heterotopic pregnancy associated with *in vitro* fertilization and embryo transfer (IVF-ET) has risen to 1%-3% of achieved pregnancies. We report a very rare case of a 32-year-old woman with 6-year primary infertility with unilateral twin tubal pregnancy and subsequent heterotopic pregnancy following two IVF treatments. Her gynecologic history was notable for previous distal occlusion of the left fallopian tube treated by laparoscopic reconstructive surgery. After ovulation induction and IVF with ET of two embryos, transvaginal sonography at 6 weeks revealed two separate gestational sacs in the left adnexal mass. Emergency laparoscopy showed unruptured ampullar pregnancy and salpingectomy was carried out. On second IVF two years later, after ovulation induction and ET of three embryos, endovaginal sonography at 6 weeks revealed only one intrauterine sac. One week later, the patient complained of intermittent episodes of lower abdominal pain in the right quadrant. Ultrasound confirmed intrauterine pregnancy and revealed right tubal gestational sac. Laparoscopy showed unruptured right ampullar pregnancy and salpingectomy was performed. Histology of salpingectomy specimens showed signs of chronic infection in both tubes. The intrauterine pregnancy progressed to term when a healthy infant was delivered vaginally. Gynecologists should always consider the possibility of ectopic pregnancy in pregnancies following IVF-ET, particularly in cases with tubal disease and abdominal pain.

Key words: *Pregnancy, ectopic – diagnosis; Fertilization in vitro – adverse effects; Pregnancy, ectopic – etiology; Pregnancy, ectopic – surgery; Pregnancy – outcome*

Introduction

Since embryo transfer (ET) does not directly involve fallopian tube, it would be expected that assisted reproductive technology (ART) might actually reduce the risk of ectopic pregnancy. Nevertheless, among women undergoing *in vitro* fertilization (IVF), 2%-5% of resultant pregnancies are tubal, a rate exceeding by 2%-3% that found in the general population[1]. However, the IVF rate may actually have decreased in recent years. Ectopic risk among ART pregnancies varied according to the type of ART procedure, reproduction health characteristics of the woman carrying the pregnancy, and estimated embryo implantation potential. In comparison with the ectopic rate (2.2%) among pregnancies conceived with IVF, the ectopic rate significantly increased when the zygote intrafallopian transfer was used (3.6%) and significantly decreased when donor oocytes were used (1.4%) or when a gestational surrogate carried the pregnancy (0.9%)[2].

Unilateral twin tubal gestations are extremely rare with a reported incidence of 1 *per* 200 ectopic pregnancies or 1 *per* 125 000 spontaneous pregnancies[3].

Correspondence to: *Assoc. Prof. Miro Kasum, MD, PhD*, University Department of Gynecology and Obstetrics, Zagreb University Hospital Center, Petrova 13, HR-10000 Zagreb, Croatia
E-mail: mkasum@gmail.com

Received April 7, 2009, accepted June 2, 2009

There are more than 100 reported twin tubal pregnancies described since 1891, generally as separate reports. Unilateral twin tubal pregnancies have been reported mostly in natural cycles and several cases after ovulation induction and IVF-ET[4].

An increased risk of combined intrauterine and extrauterine pregnancy or heterotopic pregnancy has been noted with the wider use of ovulation induction and with IVF. By multiplying the frequency of ectopic and multiple pregnancies in IVF pregnancies, an increased risk of heterotopic pregnancy associated with IVF is well established, with an incidence of 1%-3% of achieved pregnancies. The rising incidence of heterotopic pregnancy is a serious problem as the diagnosis of this potentially fatal maternal condition is often difficult due to the presence of an intrauterine gestational sac and hyperstimulated ovaries[5,6].

Case Report

A 32-year-old woman with 6-year primary infertility was referred for IVF procedure. Her gynecologic history was notable for previous distal occlusion of the left fallopian tube and laparoscopic reconstructive surgery to the ipsilateral one. She underwent ovulation induction and IVF treatment with ET of two embryos. Transvaginal sonography at 6 weeks revealed two separate gestational sacs in the left adnexal mass and a normal-sized empty uterus. Emergency laparoscopy showed an unruptured ampullar pregnancy and salpingectomy was carried out. Pathological examination identified chorionic villi with the signs of chronic infection. Two years later, the patient underwent ovulation induction and IVF with ET of three embryos. Endovaginal sonography at 6 weeks revealed only one intrauterine sac. One week later, she complained of intermittent episodes of lower abdominal pain in the right quadrant. Ultrasound confirmed intrauterine and right tubal gestational sac. At laparoscopy, an unruptured right ampullar pregnancy was found and the fallopian tube was removed. Histology of the salpingectomy specimen confirmed ectopic pregnancy with signs of inflammation. The intrauterine pregnancy progressed to term when a healthy infant was delivered vaginally.

Discussion

The major risk factors for ectopic pregnancy include tubal pathology originating from pelvic infection, endometriosis, previous surgery, and prior tubal pregnancy. Since a significantly higher rate of tubal pregnancy is found among cases with tubal factor infertility, it is postulated that among women undergoing IVF at least some of the embryos inserted in the uterine cavity migrate into the tubes. Peristaltic tubal movements then expel the embryos into the uterus. However, the presence of intratubal adhesions may disturb, delay or block this expulsion, creating tubal implantation. Along to previously damaged tubes, which may be unable to propel the embryo that has migrated into the tube back into the uterine cavity, other factors may predispose these gestations. These factors may include inadvertent placement of catheter clip, excessive force or volume during ET, and possible retrograde migration of the embryo. Other risk factors for ectopic pregnancy include patient age, cigarette smoking, prior spontaneous abortion, history of infertility and previous use of intrauterine device[6,7]. Our patient had a history of primary infertility and reconstructive surgery, and pathological examination confirmed the signs of inflammation in salpingectomy specimens of both tubes. Finally, tubal pregnancy in IVF patients with normal fallopian tubes may be associated with poor quality embryos with lower implantation capability and delayed secretion of adhesion molecules[8].

Ultrasound examination is more difficult with ART than in spontaneous pregnancies, because stimulated ovaries are much larger and can mask ectopic implantation. In addition, the adnexa are commonly pathologic (e.g., hydrosalpinx, endometriosis) and it is more difficult to identify a hematosalpinx or ectopic sac in the pelvis. The first unruptured twin tubal ectopic pregnancy was diagnosed by transabdominal ultrasound in 1986. Prior to this time, unilateral twin ectopic pregnancy was diagnosed after tubal rupture either at the time of surgery or by histopathology. In recent years, transvaginal sonography has dramatically improved the accuracy of the diagnosis of ectopic pregnancy. The introduction of high-resolution transvaginal sonography has resulted in the earlier diagnosis of ectopic pregnancy and has contributed to a recent decrease in maternal mortality and morbidity associated with this condition. Currently, transvaginal 3-D multiplanar sonography and Doppler sonography have been added to increase diagnostic potential[3,9,10].

In our patient, the diagnosis of unilateral twin pregnancy was made early by transvaginal ultrasound enabling operative laparoscopic salpingectomy in both cases.

An association between heterotopic pregnancy and IVF-ET could be expected because of the frequent occurrence of ectopic and multiple pregnancies in IVF patients. Factors like pelvic inflammatory disease, tubal surgery, hormonal induction of ovulation and transfer of multiple embryos also seem to increase the risk of combined pregnancy. Retrograde embryo migration into diseased tubes is believed to be the main cause of ectopic gestation in combination with intrauterine pregnancy following IVF. Early ultrasonography diagnosis of ectopic pregnancy in heterotopic pregnancy is often difficult due to the presence of hyperstimulated ovaries[6]. Therefore, in our patient the diagnosis was missed on initial ultrasonography. A failure to make an early diagnosis may not only lead to serious consequences for the mother, but may also jeopardize the intrauterine pregnancy. At 7 weeks of gestation, the patient was examined for sudden onset of right lower quadrant abdominal pain, when ultrasound confirmed intrauterine pregnancy and revealed right tubal gestational sac. The absence of vaginal bleeding may have been due to coexisting intrauterine pregnancy. The main issue in the treatment of heterotopic pregnancy is to be as minimally invasive as possible to preserve the development of the intrauterine pregnancy. Laparotomy is classically reserved for cases with life-threatening hematoperitoneum and hemorrhagic shock. In the largest single-center series of heterotopic pregnancies reported to date, intrauterine pregnancy proceeded to term in 50% of cases[11]. However, in terms of prognosis of intrauterine pregnancy, laparoscopic treatment was associated with favorable outcome in 62.5% of cases[12].

In our patient with double ectopic and consecutive heterotopic pregnancy following IVF-ET and with previous infertility, tubal damage and reconstructive surgery, early ultrasound was important to identify ectopic pregnancy. In case of asymptomatic patient, when the surgical approach of choice by operative laparoscopy is not considered, early ultrasonography is important to detect ectopic pregnancy. Because diagnostic difficulties in heterotopic pregnancy are well documented, it is suggested to be always included in the differential diagnosis of symptomatic patients with intrauterine pregnancy after IVF-ET. It should be remembered that if ovarian superovulation is used, the ultrasonographic presence of intrauterine pregnancy in an asymptomatic woman should not exclude the diagnosis of concurrent extrauterine pregnancy before careful ultrasonography of the pelvis. The diagnosis of the possible heterotopic pregnancy should be considered if the patient experiences abdominal pain following IVF-ET. Early transvaginal sonography performed by experienced sonographer is considered to be essential and beneficial in establishing the early diagnosis of heterotopic pregnancy. Salpingectomy can be performed as one of efficient therapies for heterotopic pregnancy with optimal outcome of intrauterine pregnancy.

References

1. The Society for Assisted Reproductive Technology Registry/ American Society for Reproductive Medicine. Assisted reproductive technology in the United States 2000 results generated from the American Society for Reproductive Medicine/Society for Assisted Reproductive Technology Registry. Fertil Steril 2004;81:1207-20.
2. CLAYTON HB, SCHIEVE LA, PETERSON HB, JAMIESON DJ, REYNOLDS MA, WRIGHT VC. Ectopic pregnancy risk with assisted reproductive technology procedures. Obstet Gynecol 2006;107:595-604.
3. PARKER J, HEWSON AD, CALDER-MASON T, LAI J. Transvaginal ultrasound diagnosis of a live twin tubal pregnancy. Australas Radiol 1999;43:95-7.
4. GOKER EN, TAVMERGEN E, OZCAKIR HT, LEVI R, ADAKAN S. Unilateral ectopic twin pregnancy following IVF cycle. J Obstet Gynaecol Res 2001;27:213-5.
5. FERNANDEZ H, GERVAISE A. Ectopic pregnancies after infertility treatment: modern diagnosis and therapeutic strategy. Hum Reprod Update 2004;10:503-13.
6. SORIANO D, SHRIM A, SEIDMAN DS, GOLDENBERG M, MASHIACH S, OELSNER G. Diagnosis and treatment of heterotopic pregnancy compared with ectopic pregnancy. J Am Assoc Gynecol Laparosc 2002;9:352-8.
7. BOUYER J, COSTE J, SHOJAEI T, POULY TJ, FERNANDEZ H, GERBAUD L, *et al.* Risk factors for ectopic pregnancy: a comprehensive analysis on a large case-control, population-based study in France. Am J Epidemiol 2003;157;185-94.
8. REVEL A, OPHIR I, KOLER M, ACHACHE H, PRUS D. Changing etiology of tubal pregnancy following IVF. Hum Reprod 2008;23:1372-6.

9. GABRIELLI S, MARCONI R, CECCARINI M, VALERI B, De IACO P, PILU G, *et al.* Transvaginal and three-dimensional diagnosis of twin tubal pregnancy. Prenat Diagn 2006;26:91-3.
10. SUMMA B, MEINHOLD-HEERLEIN I, BAUERSCHLAG DO, JONAT W, METTLER L, SCHOLLMEYER T. Early detection of a twin tubal pregnancy by Doppler sonography allows fertility-preserving laparoscopic surgery. Arch Gynecol Obstet 2009;279:87-90.
11. MARCUS SF, MACNAME M, BRINSDEN P. Heterotopic pregnancies after *in vitro* fertilization and embryo transfer. Hum Reprod 1995;10:1232-6.
12. LOUIS-SYLVESTRE C, MORICE P, CHAPRON C, DUBUISSON JB. The role of laparoscopy in the diagnosis and management of heterotopic pregnancy. Hum Reprod 1997;12:1100-2.

Sažetak

JEDNOSTRANA BLIZANAČKA TUBARNA TRUDNOĆA I SLIJEDEĆA HETEROTOPIČNA TRUDNOĆA U BOLESNICE NAKON IZVANTJELESNE OPLODNJE

M. Kasum

Jednostrana blizanačka tubarna trudnoća je iznimno rijetka s pojavnošću od 1:200 ektopičnih trudnoća. Pojavnost heterotopične trudnoće u postupku izvantjelesne oplodnje je posljednjih godina u porastu i kreće se od 1% do 3% postignutih trudnoća. Prikazujemo vrlo rijedak slučaj 32-godišnje žene sa 6-godišnjom primarnom neplodnošću s jednostranom, blizanačkom trudnoćom u jajovodu i slijedećom heterotopičnom trudnoćom nakon dva postupka izvantjelesne oplodnje. Anamnestički je ranije utvrđeno terminalno začepljenje lijevog jajovoda uz rekonstrukcijski zahvat na njemu. Nakon indukcije ovulacije i postupka izvantjelesne oplodnje te prijenosa 2 zametka, sa 6 tjedana trudnoće transvaginalnim ultrazvukom otkrivene su 2 gestacijske vreće u predjelu lijevih adneksa. Pri laparoskopiji je prikazana nerupturirana tubarna trudnoća i odstranjen je lijevi jajovod. Pri drugom pokušaju izvantjelesne oplodnje 2 godine kasnije nakon indukcije ovulacije i prijenosa 2 zametka, sa 6 tjedana trudnoće transvaginalnim ultrazvukom prikazana je intrauterina trudnoća. Tjedan dana kasnije bolesnica je dobila povremene bolove u donjem dijelu trbuha desno. Ultrazvučno je potvrđena intrauterina trudnoća, a otkrivena trudnoća u desnom jajovodu. Laparoskopski je prikazana nerupturirana desnostrana tubarna trudnoća i odstranjen je jajovod. Patohistološki su kod oba jajovoda nađeni znaci kronične upale. Intrauterina trudnoća je napredovala do termina kada je vaginalno porođeno zdravo dijete. Svaki bi ginekolog trebao razmišljati o mogućnosti izvanmaternične trudnoće nakon postupka izvantjelesne oplodnje, a naročito u slučajevima oštećenih jajovoda i bolova u trbuhu.

Ključne riječi: *Trudnića, ektopična – dijagnostika; Umjetna oplodnja – štetni učinci; Trudnoća, ektopična – etiologija; Trudnoća, ektopična – kirurgija; Trudnoća – ishod*