CASE REPORT

An unexpected triplet heterotopic pregnancy after replacement of two embryos

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We report a case of a triplet heterotopic pregnancy consisting of an intrauterine monozygous twin pregnancy and a tubal pregnancy after replacement of only two embryos in an in-vitro fertilization cycle with donor spermatozoa. This case demonstrates that sonographic demonstration of two intrauterine pregnancies after transfer of two embryos does not exclude the presence of an ectopic pregnancy. As both heterotopic pregnancy and spontaneous monozygotic twinning are more frequent after the use of assisted reproductive techniques, this combination, although extremely rare, must be kept in mind, especially in older patients with pre-existing tubal damage.

Key words: assisted reproduction/heterotopic pregnancy/monozygotic twinning

Introduction

It is known that the incidence of heterotopic pregnancy, defined as a combined intrauterine and extrauterine pregnancy, has increased since the use of ovarian stimulation and the advent of assisted reproductive techniques (ART) and is estimated to have an incidence of ~1% (Tal et al., 1996). The incidence of monozygotic twinning is also increased following in-vitro fertilization (IVF) and can be estimated at 1.33%, if the estimated incidence of 0.42% after in-vivo fertilization is accepted (Edwards et al., 1986).

The incidence of the combination of heterotopic pregnancy and monozygous twinning following ART, can be calculated as the product of both incidences or 1%×1.33% = 0.0133%. To our knowledge, this is the first report to illustrate the coexistence of both rare phenomena, namely a heterotopic pregnancy, consisting of an intrauterine monozygous (i.e. vanishing) twin and a tubal pregnancy occurring after replacement of only two embryos, in an IVF cycle where donor spermatozoa was used.

Case report

A 30 year old woman, known to have polycystic ovary syndrome (PCOS), was referred to our centre with a request for artificial insemination using donor spermatozoa (AID). During ovulation induction, she developed ovarian hyperstimulation syndrome (OHSS), complicated by acute torsion of the right ovary, which was unwound during laparotomy. Since AID remained unsuccessful, she was offered IVF using donor spermatozoa (IVF-D). In the fourth cycle, one day after embryo transfer, a laparoscopy was performed because of an acute abdominal pain and a second torsion of the right ovary was diagnosed and unwound laparoscopically. This cycle resulted in an uneventful twin pregnancy and vaginal delivery.

The patient returned with a second request for IVF-D two years later. In the third cycle she became pregnant after transfer of two embryos, one of excellent and one of good quality, both at the 8-cell stage, replaced 72 h after oocyte retrieval. On day +12 after embryo transfer, the serum human chorionic gonadotrophin (HCG) measurement was 231.3 mIU/ml.

The patient presented with low abdominal pain in the right iliac region 25 days after embryo transfer. Transvaginal sonography showed two gestational sacs, corresponding to five weeks of amenorrhoea, although one gestational sac was smaller than the other (diameters of 16 and 12 mm respectively). The ovaries had a multicystic luteal aspect, as seen after ovarian stimulation. A diagnosis of a gastrointestinal infection was considered because of the simultaneous presence of diarrhoea and vomiting.

By 39 days after transfer, the patient no longer complained of any pain. Sonography again showed two intact gestational sacs, each containing one embryo with a crown–rump length of 15 mm, corresponding to eight weeks of amenorrhoea (Figure 1). Only one embryo showed cardiac activity. The ovaries were large and multicystic.

After three days she presented with painless vaginal bleeding. Sonography revealed a disappearing gestational sac with a non-viable embryo and an ongoing gestation with cardiac activity. The diagnosis of a vanishing twin was made and the bleeding was attributed to this phenomenon.

However, on the 47th day after embryo transfer, the patient showed signs of acute abdominal pain and a tender mass could be palpated in the right fossa. Sonography reconfirmed the existence of a vanishing twin and a right ovarian cyst of 8 cm in diameter. A preoperative differential diagnosis was made between a haemorrhagic corpus luteum cyst, a third torsion of the right ovary or a heterotopic pregnancy. Laparoscopy was performed and showed an haemorrhagic adhesion of the right tube and ovary. A site of rupture was seen at the right tubal wall. The complete right adnex was removed by laparotomy.
and sent for pathological examination. The existence of decidual tissue with trophoblastic villi in the right tube confirmed the diagnosis of ectopic pregnancy (Figure 2). The patient recovered uneventfully. She was given i.m. injections of progesterone in oil, 100 mg daily, until 12 weeks of amenorrhoea. Repeated ultrasound examination revealed one viable embryo and an almost completely vanished second gestational sac. The pregnancy continued with no further complications and the patient was delivered vaginally of a healthy boy.

Figure 1. Intrauterine monozygotic vanishing twin, arrow head = ongoing pregnancy; arrow with shaft = vanishing pregnancy.

Figure 2. Placental villus located in the lamina muscularis of the Fallopian tube. Bar = 100 μm.

Discussion
To our knowledge this is the first report of a heterotopic IVF pregnancy consisting of an ectopic tubal pregnancy and an intrauterine (vanishing) twin after replacement of only two embryos.

Monozygosity of the intrauterine twin was assumed because the number of pregnancies exceeded the number of embryos replaced. Delayed ovulation of a remaining follicle with subsequent spontaneous fertilization after coitus near the time of ovulation was excluded because of the use of donor spermatozoa. Histopathological confirmation of monozygosity was impossible because of the evolution to a vanishing twin pregnancy.

Although monozygotic twinning is a relatively rare event in in-vivo conception, estimated to occur in 0.42% of all births (Bernischke, 1961), it has been suggested that its incidence is increased in IVF pregnancies. The estimated incidence of monozygotic twinning in IVF conceptions is 1.33% (Edwards et al., 1986). Monozygosity seems to occur more frequently in older women (i.e. >32 years of age), possibly because of a gradual decrease in the average thickness of the zona pellucida with increasing maternal age (Cohen and Feldberg, 1991). In this patient, who was 32 years old, a family history of monozygotic twinning was present.

Heterotopic pregnancy, defined as a combined intrauterine and extrauterine pregnancy, is a rare event whose incidence has increased with the use of ovarian stimulation and the advent of ART. Reports in the literature show an incidence of heterotopic pregnancy of ~1% for classical IVF procedures (Tal et al., 1996).
Factors predisposing for heterotopic pregnancy appear to be identical to those predisposing for ectopic pregnancy. The main factor is believed to be tubal damage after pelvic inflammatory disease, endometriosis or former tubal surgery. One possible explanation is that transferred embryos which migrate into the damaged tubes are not expelled by peristaltic movements (Goldman et al., 1992; Tal et al., 1996). In this case the tubal damage may have been due to the previous torsions of the right adnex (the side of the ectopic pregnancy) and the subsequent surgical procedures. Mechanical and ischaemic damage to the tube during torsion and surgery may have caused adhesions and distortion of the tubal function thereby augmenting the chance of tubal implantation. Other contributing factors, including the use of gonadotrophins, deep insertion of the catheter during transfer, the amount of fluid used as a medium for the embryos and the high number of embryos transferred, have been suggested but not confirmed in a recent review by Tal et al. (1996).

The clinical diagnosis of heterotopic pregnancy can be very difficult. Usually the clinical signs of the extrauterine pregnancy predominate. Abdominal pain is the most frequent symptom appearing in 82.7% of heterotopic pregnancies (Tal et al., 1996). The introduction of transvaginal sonography to daily practice has increased the likelihood incidence of preoperative diagnosis. According to Tal et al. (1996), sonographic diagnosis of a heterotopic pregnancy was made in 41.1% of cases. However, we share the opinion of Thakur and El-Menabawey (1996), that the use of ovarian stimulation with gonadotrophin often limits an adequate evaluation of the adnexal region. In our case no extrauterine pregnancy was seen by vaginal ultrasonography. The diagnosis of ectopic pregnancy was made during laparoscopy, although the diagnosis of an ectopic pregnancy had been considered preoperatively.

Therapy should aim at terminating the extrauterine gestation with minimal distress for the intrauterine pregnancy. The most common technique has been salpingectomy through laparotomy. However, less invasive techniques are gaining field. These include: laparoscopic salpingectomy and laparoscopic aspiration of the trophoblast tissue from the pregnant tube (Guirgis, 1990). Injection of potassium chloride and even methotrexate into the pregnant tube has been performed for the treatment of a heterotopic pregnancy (Guirgis, 1990). We decided to remove the adnexal mass by laparotomy. A laparoscopic approach was contra-indicated by the intrauterine pregnancy, as well as by the presence of a haemoperitoneum and adhesions.

The prognosis for the intrauterine gestation after treatment of the ectopic pregnancy is good. Of such pregnancies, 50–100% progress normally (Marcus et al., 1995). In this case, the remaining singleton pregnancy continued with no further complications.

We conclude that, when ART are used, this extremely rare combination (calculated incidence: 0.0133%) must be kept in mind, especially in older patients with pre-existing tubal damage. The fact that two intrauterine pregnancies are seen by ultrasound after replacement of two embryos does not exclude the presence of an ectopic pregnancy. Careful examination of the pelvis by vaginal ultrasound is absolutely necessary in all patients.

References

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