CASE REPORT

Bilateral simultaneous tubal sextuplets: pregnancy after in-vitro fertilization–embryo transfer following salpingectomy

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The presence of a damaged tube has been suggested in recent studies to have a negative effect on in-vitro fertilization (IVF) outcome. Performing bilateral salpingectomy prior to IVF to maximize pregnancy rates may also result in unnecessary surgery. This case is also an example of the occurrence of interstitial pregnancy after salpingectomy. This unusual type of ectopic pregnancy must be kept in mind when evaluating a patient suspected of a possible early abnormal gestation after assisted reproductive technologies.

Key words: ectopic pregnancy/interstitial/in-vitro fertilization (IVF)/salpingectomy/sextuplets

Introduction

The first pregnancy reported after in-vitro fertilization and embryo transfer (IVF–ET) was ectopic (Steptoe and Edwards, 1976). The incidence of ectopic pregnancy after assisted reproductive technologies varies from 2 to 11% and is significantly higher than in a normal population (0.8%). It is becoming clear that some of the previously very rare types of ectopic pregnancies are much more common following assisted reproduction.

The first case of bilateral ectopics following IVF–ET was confirmed in 1985 (Hewitt et al., 1985). It is estimated to occur in about 1 of 1500 ectopic pregnancies (Olive et al., 1988; Rizk et al., 1990). In this presentation, we discuss an unusual case of simultaneous bilateral sextuplets following IVF. Puttemans and Brosens (1996) raised concern about the indiscriminate use of preventive salpingectomy prior to IVF. Our rare interstitial triplet pregnancy following IVF–ET occurred after salpingectomy represents the negative effect of uncontrolled surgery to the Fallopian tube.

Case report

The patient was a 30 year old female with a chlamydia titre of 1:128 which was treated with doxycycline and with left tubal fimbrial phimosis, which was managed with fimbrioplasty and adhesiolysis through laparoscopy in 1995. Although a spontaneous pregnancy ensued then, it was a left ampullary pregnancy and was treated elsewhere by left salpingectomy in 1995.

Hysterosalpingography (HSG) showed that the right Fallopian tube was patent, while the left Fallopian tube appeared to be blocked at the proximal end. The patient was treated by ovulation induction with clomiphene–human menopausal gonadotrophin (HMG) followed by intrauterine insemination (IUI) for several cycles. Subsequently, after supportive counselling, the patient opted to undergo IVF. In July 1996, she was stimulated with a total of 21 ampoules of follicle-stimulating hormone (FSH; Metrodin®, Laboratoires Serono SA, 1170 Aubonne, Switzerland) after suppression with 1.87 mg leuplin depot (Takeda Chemical Industries Ltd., Osaka, Japan), i.m. from the mid-luteal phase of the previous cycle. Human chorionic gonadotrophin (HCG; Pregnyl®, Organon, Oss, The Netherlands), 10 000 IU, was given when the largest follicles were 18 mm in diameter and the oestradiol concentration was 3600 pg/ml. In transvaginal oocyte retrieval, 29 oocytes were obtained. Six embryos with normal fertilization and cleavage were transferred 2 days later after consultation about multifetal risk. Luteal phase support was with HCG, 2500 IU i.m., from the day of embryo transfer followed by two doses at three-day intervals and 600 mg utrogestan (Labo Piette International N.V., 1620 Drogenbos, The Netherlands) daily from the day after ovum retrieval. Pregnancy was indicated by an HCG level 2 weeks later of 226 mIU/ml.

On the 25th day after embryo transfer she developed acute lower abdominal pain and vaginal spotting. The serum HCG level was 3150 mIU/ml. However, ultrasound showed no gestational sac within the uterine cavity, but the presence of large bilateral cystic ovaries with an increased ovarian diameter >10 cm each and a large amount of intra-abdominal fluid. She was admitted to the hospital with the diagnosis of ectopic pregnancy and ovarian hyperstimulation syndrome (OHSS). The basis for the diagnosis of the latter was the high oestradiol level, multiple follicles, large bilateral cystic ovaries with increased diameter and a large amount of fluid. The patient was kept on strict bedrest and daily blood samples were obtained for HCG assessment and to monitor the severity of the OHSS. Five days later the HCG rose to 6350 mIU/ml, and the haemoglobin concentration showed a decrease of 1g/100 ml. The ultrasound demonstrated three gestational sacs in the right adnexae with no pregnancy in the uterus (Figure 1). The
Bilateral sextuplets after IVF–ET

Figure 1. Ultrasound image of three gestational sacs at right adnexa.

Figure 2. Bilateral sextuplet pregnancy with, right, ampullary triplets and, left, interstitial triplets.

patient consented to surgical intervention and a laparoscopy was performed.

On laparoscopy, the patient was noted to have a $3\times2$ cm ampullary mass on the right side and a $2\times2$ cm cornual protrudent mass on the left side (Figure 2). Right salpingectomy was performed, using the technique previously described (Dubuisson et al., 1987). A longitudinal incision was made at the apex of the left cornual mass and the products of conception were found at the site of the incision. Left cornual enucleation was performed and the incision site was left open for primary closure. The patient did well postoperatively and was discharged 3 days later, with the βHCG titres falling to 715 mIU/ml 3 days later and returning to zero over the next 2 weeks.

Pathological examination demonstrated separated chorionic villi and blood clots consistent with triplets from the right-sided tube and well encapsulated gestational tissue consistent with triplets in the specimens from the interstitial position of the left-sided tube. No additional pathology was noted in the specimens. However, the zygosity of this multiple gestation was not further determined by using DNA probes.

Discussion
A case of a unilateral triplet pregnancy was reported by Demick et al. (1958). The first bilateral simultaneous pregnancy following natural conception was reported by Abrams et al. in 1948. The unusual types of ectopic pregnancies are much more common in assisted reproduction. The first case of
bilateral ectopics following IVF–ET was reported by Hewitt et al. (1985) and a case of bilateral ectopic pregnancy after gamete intrafallopian transfer (GIFT) by Olive et al. in 1988. Since then there have been few such reports in the literature.

Chlamydia trachomatis is one of the most frequent sexually transmitted pathogens. This organism can cause symptomatic and asymptomatic infections of the female urogenital tract. Repeated pelvic inflammatory disease (PID) can lead to tubal damage, but tubal infertility is not necessarily related to a history of symptomatic PID (Dieterle and Wollenhaupt, 1996). Tubal factor infertility remains the most common indication for in-vitro fertilization and encompasses multiple aetiologies, including unilateral or bilateral hydrosalpinx, distal or proximal obstruction and intraluminal or extraluminal adhesions.

The risk factors associated with ectopic pregnancies after IVF–ET are conflicting. In tubes that are normal, the transferred embryos return from the tube to the uterine cavity, simulating the physiological journey of the fertilized ovum. This transport may be thwarted when the tubes are dysfunctional, and hence favour ectopic implantation. Some authors have also reported 100% pathological lesions in their series of ectopic pregnancies, even when IVF had been performed for endometriosis or unexplained infertility. Tubal damage may be a major risk factor in development of an ectopic pregnancy after IVF–ET. Risk factors in assisted reproductive technology (ART) for ectopic pregnancies include sexually transmitted disease, known tubal damage and prior distal tubal surgery (Zouves et al., 1991).

In this case the replacement catheter was inserted once only and all six embryos were expelled simultaneously. There are three theoretical mechanisms to account for the occurrence of a bilateral tubal pregnancy following such a single transcervical multiple embryo replacement. Firstly, correctly replaced intrauterine embryos may have migrated into both sides sometime after replacement, as a result of the reflux of uterine secretions. Secondly, due to a ‘spray effect’, it is possible that with the catheter tip correctly positioned in the uterine cavity, embryos were directly injected into both sides simultaneously, when the embryo replacement syringe was emptied. Thirdly, the embryos may have been directly injected into the right Fallopian tube as a result of faulty replacement technique, with three embryos subsequently migrating from the site of replacement, traversing the uterine cavity, entering and then implanting in the interstitial part of left tube. It is not possible to find out which of these three possibilities occurred on this occasion.

The mechanisms by which hydrosalpinx may affect IVF success include reflux of hydrosalpinx fluid into the uterine cavity, endometrial damage simultaneous with tubal damage or by alteration of endometrial integrin expression (Strandell et al., 1994). All these mechanisms can affect endometrial receptivity, leading to implantation failure. It was originally thought that the risk of ectopic pregnancy could be eliminated by removing both Fallopian tubes (Steptoe and Edwards, 1976). However, even when the tubes are excised, there still remains a risk of interstitial pregnancy. Our rare case of a triplet interstitial pregnancy occurred after salpingectomy and represents the negative effect of uncontrolled surgery to the Fallopian tube. It is well known that salpingectomy itself increases the risk of interstitial pregnancy. Salpingectomy should only be considered if salpingoscopy demonstrates severe pathology of the ampullary mucosa and a thick wall due to chronic inflammation (Puttemans and Brosens, 1996).

To our knowledge, no case reports of bilateral multifetal ectopics have included a genetic analysis of the embryos to evaluate their zygosity. Without genetic analysis, determination of multiple gestational zygosity usually relies only on visual comparisons of the embryos. These conventional criteria include the size of embryos, the developmental stages of fetuses, the number of corpora lutea and the separated fetal membranes. Whereas careful observation provides only a subjective determination of zygosity, genetic analysis objectively and accurately distinguishes zygosity. Analysis of a sufficient number of genetic markers allows calculation of a probability close to 100%.

Intrauterine insemination, in combination with ovarian stimulation using gonadotrophins, has been introduced as an acceptable method for the treatment of infertility of different causes. Failure to conceive can be regarded as a problem of gamete quality and interaction, embryo development and transportation in the preimplantation stages, or implantation and subsequent development. The use of IVF is recommended not only for therapeutic reasons, but also because of the possibility of learning about the reproductive processes of the infertile couple. In most IVF centres, multiple embryo replacement is performed to maximize the success rate. As a consequence, a concomitant increase in the incidence of multiple pregnancies is observed, associated with substantially more medical and psychological problems. In some countries, the number of embryos to be transferred has been regulated through legislation. Unfortunately, this also lowers the overall chances of success in achieving pregnancy in any individual cycle, and promotes the necessity for recurrent cycles of hormonal stimulus and follicular aspiration, procedures not without risk. From a clinical point of view, the decision on the number of embryos to transfer should be reached with the input of the laboratory personnel, the couple, and the attending clinician. When this patient was given six embryos instead of three or four, this number was not chosen at random. There were several predisposing factors, including the large number of embryos available for transfer, a poor outcome in previous cycles and the decision-making of the couple.

It has been reported that multiple embryo transfer and ovarian stimulation may also be risk factors for ectopic pregnancy, but this has been disputed (Dubuisson et al., 1991). Our patient had three risk factors, a positive chlamydia titre, tubal damage, and prior reconstructive surgery. It is now generally recommended that the number of transferred embryos should not exceed three, especially in women with a history of tubal damage. This preventive measure may provide some protection, especially for high risk patients.

References


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