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Simultaneous Bilateral Tubal Ectopic Pregnancy after Intracytoplasmic Sperm Injection and Embryo Transfer, in a Patient with Stage 3 Endometriosis

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Abstract

Objective: To describe a simultaneous bilateral tubal ectopic pregnancy after intracytoplasmic sperm injection and embryo transfer: A case report.**Setting:** Department of Reproductive Medicine, Femme-Mère-Enfant University Hospital, Bron, France.**Introduction:** The incidence of extra-uterine pregnancy increases to 2% to 12% following IVF-ET; several pathogenic theories have been suggested, including abnormal hormonal secretion or exogenous hormones administered in assisted reproductive technology (ART).**Patient and method:** A 32-year-old nulliparous woman, with primary infertility and endometriosis stage 3, was treated by ART with intracytoplasmic sperm injection and embryo transfer.**Result:** The patient showed simultaneous bilateral extra-uterine pregnancy, managed by laparoscopic salpingectomy.**Discussion:** The various possible pathophysiological mechanisms are described, with a review of the literature on simultaneous bilateral extra-uterine pregnancy following ART.**Conclusion:** In pregnancies following ART, ectopic pregnancy should always be screened for by serum hCG monitoring and transvaginal ultrasound until the implantation site can be confirmed, as incidence is higher than in spontaneous pregnancy. Even if serum hCG concentration increases normally, possible bilateral EP should always be investigated if no intrauterine gestational sac can be seen.

Introduction

The rate of ectopic pregnancy (EP) is 2% of all pregnancies, and higher in case of assisted reproductive technology (ART). In the USA in 1999, EP was found in 2.2% of all pregnancies from *in vitro* fertilization (IVF) and in 1.9% of those from intracytoplasmic sperm injection (ICSI), and in France in the same year in 3.4% and 1.9% respectively [1]. Steptoe and Edwards reported the first case of EP after IVF and embryo transfer (ET) in 1976 [2]. Bilateral tubal pregnancy is a rare clinical condition with an incidence of 1 in 200,000 pregnancies [3,4], and is very rare after ART, with only a few case reports: in 1983, Trotnow et al. reported the first case after IVF-ET [5], and Kahraman et al. the first case after ICSI, in 1995 [6].

The present case of bilateral tubal pregnancy occurred in a patient undergoing ICSI with embryo transfer (ET) in day 2 after ICSI for infertility secondary to grade-3 endometriosis, with isolated asthenospermia as a male factor.

Patient and Method

A 32-year-old G1P0 woman had history of first trimester miscarriage in 2011, and grade-3 endometriosis discovered in 2009 during diagnostic laparoscopy for dysmenorrhea, with removal of a 6 cm ovarian cyst; methylene blue dye test was positive bilaterally, demonstrating tubal permeability. She had been consulting in our infertility clinic in 2013 for secondary infertility for 2 years since the early miscarriage in 2011. MRI showed recto-vaginal nodular adhesion with left ovary endometrial cyst. Serology (chlamydia, mycoplasma) was negative and anti-Müllerian hormone (AMH) concentration was 4.66 ng/ml. On the other side, there was isolated asthenospermia as a male factor.

It was decided to perform down-regulation with GnRH agonist from day 21 of the last menstrual period (Decapeptyl, 0.1 mg[®]), followed by recombinant follicle-stimulating hormone stimulation (Puregon Pen[®], 300 IU). Thirty-six hours after induction of ovulation by human chorionic gonadotropin (hCG: Ovitrelle[®]) on day 12 after stimulation, egg collection retrieved 10 oocytes. Two embryos were transferred in day 2

Keywords: Bilateral ectopic pregnancy; IVF; ICSI; ET; Endometriosis

after ICSI by a Ellios catheter in 15 μ l transfer medium and 2 embryos was frozen at the blastocyst stage (days 5 and 6). The luteal phase was supported with progesterone (Utrogestan[®], 600 mg per day). On day 15 after ET, hCG concentration was 242 IU/L and 1,383 IU/L 48 h later.

Results

The patient presented in the gynaecology emergency department 19 days after ET for right iliac fossa pain without vaginal bleeding. hCG was 2,377 IU/L and vaginal ultrasound found no intrauterine gestational sac, lateral uterine mass or free fluid in the recto-uterine pouch; the only positive finding was the 40 mm right ovarian endometrial cyst, which had been known for 1 year. The patient was admitted for observation. At 48 h, hCG concentration was 7,722 IU/L, and control ultrasound showed free fluid and a 10 mm left adnexal mass (Figure 1).



Figure 1 Ultrasound image of the left side ectopic pregnancy

Laparoscopic left salpingectomy was immediately performed for left ampullary EP and moderate bleeding; the right tube was slightly distended with important adhesions and impossibility to differentiate if there was another EP, and was therefore conserved, with postoperative hCG monitoring. The patient was discharged on day 1 after surgery in good condition with a decreased level hCG at 3,780 IU/L.



Figure 2 Ultrasound image of the right side ectopic pregnancy

48 hours after discharge, her hCG level was 1,980 IU/L. One week later, she consulted again in the emergency department with right iliac fossa pain with guarding and no rebound tenderness, associated with mild vaginal bleeding. Ultrasound

found a 4-mm right adnexal mass and free fluid (Figure 2); hCG concentration was 3,520 IU/L. Laparoscopic right salpingectomy was performed for distended right tubal EP and severe bleeding.

The patient was discharged on postoperative day 2 in good condition with hemoglobin at 9 g/L and serum hCG at 1,103 IU/L (returning to zero 2 weeks after discharge); histopathological examination confirmed bilateral tubal pregnancy.

Discussion

There are several theories about the genesis of EP and its physiopathology is well known: endosalpinx lesion (tubal factor) is one important factor [7-10], induced by sexually transmitted infection, distortion of pelvic anatomy caused by diseases such as endometriosis or by adhesion after previous surgery, history of EP or hormone concentration imbalance during the menstrual cycle [11].

Incidence in IVF-ET increases to 2% to 12% [12,13], and seems to be related to abnormal hormonal secretion or exogenous hormones administered in ART (notably the smooth muscle relaxant effects of progesterone in luteal support [14]; incidence may increase with the number of transferred embryos [15]; the volume of transfer medium may also be implicated, and it is recommended that it should not exceed 20 μ l [16]. Dubuisson et al. [8] reported a 2% incidence of EP after embryo transfer in 10 μ l to 20 μ l of fluid, although other authors did not confirm these findings [17,18]. Knutzen et al. [19] reported tubal reflux in 38% of patients undergoing mock transfer of 40 μ l of radiopaque dye.

In the particular case of bilateral EP after ART, three theories have been suggested. Firstly, embryos may be directly injected into the tubes. Secondly, embryos may be transferred correctly to the endometrial cavity but regressively migrate to the tubes as consequence of endometrial secretion. The third theory involves a "spray effect" during transfer whereby embryos might be pushed toward the tubal portions; in healthy functioning tubes, however, they should return to the endometrial cavity, further suggesting that tubal impairment can increase EP risk [11,20,21].

The present case involved no EP risk factors other than ART and advanced endometriosis; the latter plays an important role in increasing the probability of EP, causing intrinsic tubal pathologies such as tubal endosalpingiosis that may also account for EP.

Conclusion

Ectopic pregnancy after *in vitro* fertilization is becoming more frequent with the development of assisted reproductive technology. In case of pregnancy after ART, EP should always be screened for by serum hCG monitoring and trans-vaginal ultrasound until the implantation site can be confirmed, as incidence is higher than in spontaneous pregnancy. And in case of transfer of 2 embryos we should be careful even if serum hCG concentration increases normally, possible bilateral EP

should always be investigated if no intrauterine gestational sac can be seen: in the present case, serum hCG levels were doubling normally, but there was no intrauterine image. Another important point during ART is that, in case of unilateral EP, the situation of the other tube should be systematically checked and hCG levels should be monitored until negative; in the present case, distention of the other tube was mild; but, as the patient was known to have severe endometriosis with several peritoneal adhesions, it was decided to continue hCG monitoring, which decreased after the first operation but then increased one week later.

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