A case report of bilateral tubal ectopic pregnancy following day 5 embryo transfer

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The incidence of ectopic pregnancy after in vitro fertilization (IVF) ranges from 2.1 to 9.4 of all clinical pregnancies [1]. Bilateral tubal pregnancy is a rare clinical condition which occurs in only 1 per 200,000 pregnancies [2].

We present a case of bilateral tubal pregnancy in a woman who underwent IVF treatment, in whom three morulae were transferred.

A 35-year-old woman who had a 17-year history of primary male factor infertility was admitted with complaints of abdominal pain and vaginal bleeding. She had been treated with two cycles of controlled ovarian hyper-stimulation plus intrauterine insemination. Additionally, the patient underwent two cycles of intracytoplasmic sperm injection (ICSI) with the standard long protocol the previous year.

In the first ICSI cycle, two 4-cell grade A (excellent grade) embryos were transferred 48 h after oocyte injection. In the second ICSI cycle, three embryos were transferred 48 h following oocyte injection. Those transferred in the second cycle consisted of two 4-cell grade A embryos and one 4-cell grade B embryo. The patient had regular menstrual cycles with no history of pelvic inflammatory disease. Bilateral tubal patency was revealed on hysterosalpingography and hysteroscopy was normal.

Because of repeated implantation failures, the patient elected to undergo an ICSI blastocyst transfer. She was treated with the standard long protocol as previously mentioned [3]. Ten oocytes were retrieved, of which six were fertilized and cleaved. Three morula stage embryos were transferred 120 h after injection. A soft embryo transfer (ET) catheter (Labotect GmbH; Göttingen, Germany) was used to transfer the embryos, which was done without complications. The luteal phase was supported with vaginal progesterone (Abureihan Pharmaceutical Co, Tehran, Iran), 400 mg twice daily until the day of the β-hCG assay. Two weeks after ET, the patient's β-hCG level was 639 mIU/ml. She experienced vaginal bleeding and pain 2 weeks following ET.

Upon admission, she had left lower abdominal pain with a blood pressure of 125/80 mmHg and a heart rate of 80 beats per minute. An ultrasound revealed a 23 mm × 18 mm left adnexal mass, suggestive of ectopic pregnancy, and a small amount of fluid. Endometrial thickness was 7 mm and the uterine cavity was empty. Laparoscopy was performed, which revealed a 3 cm unruptured left ampullary ectopic pregnancy. A left linear ampullary tube salpingostomy was done. Inspection of the right tube showed a bulging area in the ampullary region. Linear salpingostomy was

performed and an ectopic product of conception was seen in both sides. Pathology confirmed placental villi in the right and left tubes. The patient was discharged home the following morning, in good condition.

Risk factors for ectopic pregnancy after IVF are still unclear and there is a gap in our learning about the reasons and mechanisms of implantation of embryos in the oviduct [4]. Double blastocyst transfer [5] is reported as a risk factor for ectopic pregnancy following IVF.

The mammalian oviduct is created from heterogeneous cell types such as ciliated and secretary epithelial cells, and smooth muscle cells. Many studies have shown that ciliary beating and smooth muscle activity are the most common factors responsible for moving the embryo through the oviduct [6]. The coordination of embryo-oviduct epithelial cell interaction plays a role in this process and abnormalities in this interaction may change the homing of the embryos in the oviduct [6].

Bilateral ectopic pregnancy is rare [2]. There are several theories which explain this condition, one of which is the "spray effect theory" that the transfer medium may lead embryos in separate directions towards the tubes. It is more likely to occur when a larger volume of transfer medium is used [7].

The likelihood of bilateral tubal pregnancy is not only due to embryos reaching the tubes, but may be an additional pathological event that prevents their movement back to the uterus. A potential mechanism may be the result of tubo-peritoneal disease and the embryo itself. Tubo-peritoneal disease can interfere with tubal motility [8].

Blastocyst transfer has a higher implantation rate when compared to the cleavage stage transfer [9]. This would imply that the blastocyst which reaches the tube may have a higher chance of implantation. A significant difference in the ectopic pregnancy rate was found between single and double transfers when frozen blastocyst transfers were performed [5]. However, Milki *et al.* [10] found no differences in ectopic pregnancy rates with day 3 vs. day 5 embryo transfers.

Radical or conservative surgery and medical managements are different options for treating tubal EP. Despite the possibility of higher incidence of ectopic pregnancy in patients with linear salpingostomy, we elected to do it as even IVF is associated with ectopic pregnancy. The patient was advised accordingly, and after considering risks and benefits, a conservative approach was finally resorted to.

The patient described in this case report had no risk factors for ectopic pregnancy with the exception of the transfer of three embryos. Because of the higher incidence of ectopic pregnancy in assisted reproductive technology (ART) cycles, a high index of suspicion and early intervention are mandatory. When a diagnosis of ectopic pregnancy is made, both adnexa should be examined in order to prevent maternal morbidity and mortality. Reducing the number of transferred embryos can lessen bilateral tubal pregnancies.

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