Tubo - ovarian pregnancy following in vitro fertilization - embryo transfer: A case report and review of the literature.

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Abstract

Heterotopic pregnancy (HP) is a rare event of ectopic pregnancy after natural pregnancy or assisted reproductive technology (ART) procedures, and its pathophysiologic mechanisms have not been clarified. Moreover, it is difficult to diagnose an HP due to the rarity and the asymptomatic nature. Here we present a case of an unexplained infertility woman following in vitro fertilization - embryo transfer (IVF - ET) developed HP — intrauterine pregnancy and tubo - ovarian pregnancy, and managed conservatively by laparoscopic. HP after ART represents an emergency and therefore the intrauterine pregnancy and the fertility potential will be better preserved by improved sonographic imaging and experienced surgical hands.

Keywords:

Heterotopic pregnancy; ovarian pregnancy; assisted reproductive technology; in vitro fertilization - embryo transfer.

Introduction

Heterotopic Pregnancy (HP) is a very rare event of ectopic pregnancy with a reported incidence of from 1 in 30,000 to 1 in 7,000 naturally conceived pregnancies [1]. However, there is an high increasing in the incidence of HP [2], which increased up to 1% ˜ 3% in all ectopic pregnancies [3], as the consequence of the improvements of assisted reproductive technology (ART), the rising number of pelvic inflammatory disease (PID) and more frequent performance of tubal surgery among females. But the mechanisms still have not been clarified. On the other hand, HP—intrauterine pregnancy and tubo - ovarian pregnancy following in vitro fertilization (IVF) is even more rare and no case has been reported in literature.

We present a case with intrauterine pregnancy and tubo - ovarian pregnancy. The pregnancy was achieved by ovarian stimulation followed by in vitro fertilization - embryo transfer (IVF - ET). The mechanism of the rare event is not completely clear.

Case Report

A 28-year-old women (gravida 0 para 0), was admitted on a suspected HP to our hospital 79 days after IVF - ET, who was asymptomatic before her arrival. She had gone through 2 laparoscopic surgeries for appendicitis and intestinal tuberculosis (10 years ago), and oral anti-tuberculosis drug had 6 months for pulmonary tuberculosis (9 years ago). Endometrial curettage was performed due to infertility 4 years ago and pathological examination showed tuberculosis endometritis. 2 months ago, Sheundergone controlled ovarian hyperstimulation (COH) and 2 fresh embryos were transfered 11 weeks before her admission.

One month after embryo transfer (ET), transvaginal ultrasound in other hospital showed an intrauterine gestational sac, but another month later, showed an intrauterine pregnancy (equivalent to14 weeks gestation) and a suspected abdominal pregnancy. Repeated on admission ultrasound revealed an enlarged uterus with

an intrauterine gestational sac and a hypo echogenic mass in left posterior of cervical canal measuring 12.4 x 9.22 x 6.27 cm and an ectopic gestational sac-like structure contained a fetal pole with active fetal heart movement (equivalent to 13 weeks gestation) within the mass (Figure 1).

On her admission, there was no any symptoms or signs, and hemodynamically stable. However, an acute abdominal pain suddenly occurred, and an emergent laparoscopic surgery was managed. Intraoperative laparoscopic evaluation revealed that, dense omentum and bowel adhesion from previous incision, approximately 100 ml of hemoperitoneum. Right adnexa area looked normal. As figure 2 shown, left oviduct ampulla looked larger and swollen. The amniotic fluid was extracted from the weak and bright area of the ampulla by puncture, and the fetus disassociated from the fallopian tube (the size be of 13 weeks gestational). The umbilical cord was cut and gradually separated, and saw the umbilical cord connected between the tubal fimbria end and the left ovarian cortex. A fresh placenta attached to the left ovary. The uterus was large as 13 weeks gestation. Then, the diagnosis of a tubo - ovarian pregnancy was established. Laparoscopic ovarian wedge resection and left tubal resection were performed.During the operation, the left fallopian tube and ovary was brittle and easily bleed. There was about 2,000 ml blood loss during the surgery. The patient transfused 6.5 units suspension red blood cells and 200 ml plasma. She was discharged 5 days after the operation. Pathological examination confirmed the diagnosis (Figure 3). The patient experienced term delivery and then in contraception status.

Discussion

The simultaneous occurrence of both intrauterine and extrauterine pregnancy is defined as HP. Generally, there are two types of HP — synchronous and non-synchronous,the later is relatively rare. If the two zygotes are fertilized at the same time, or one zygote divided into two blastomeres, then they are respectively implanted in the uterine cavity and extrauterine cavity. The embryonic development is synchronous. It is called the synchronous HP. Once the zygote is embedded in the uterine cavity, a higher serum β - human chorionic gonadotropin (β - hCG) level could promote the follicular development, ovulation. Then the egg meets with the sperm, which is from a tract between epichorion and decidua basalis, and a fertilization process was completed in the tubal. It is called the nonsynchronous HP, but tubal peristalsis has a decrease during the process of fertilization. In our case, we speculated that it could be a synchronous HP due to there were two embryo transferred at the same time and there was no difference in the gestational age between the intrauterine and ectopic pregnancy. For a nonsynchronous HP, the intrauterine pregnancy is more early than the ectopic, which may lead to the misdiagnosis or missed diagnosis of HP.

HP is a rare form of pathologic pregnancy, fallopian tube is the most common sites, and few cases be seen in the ovary [4]. In this case, HP — intrauterine pregnancy and tubo-ovarian pregnancy following IVF is even more rare and no case has been reported in literature. The question coming in mind is where the implantation sites in? The ovary or the tubal?

After once more review the case and literature, We thought the implantation site may be in fallopin tube. Among the genital organs affected by mycobacterium tuberculosis, fallopian tubes are quite common [5].In morphology, infected genital organs varies widely. The tubal ampulla presents the earliest changes, the fimbrial processes turn into swollen later. The pathological changes of TB endometritis include endometrial ulceration, caseous necrosis, haemorrhage, and adhesions may occur between ovaries and adjacent pelvic organs leading to adnexal mass [6]. The female infected genital organs can lead to infertility, menstrual irregularities, ovarian cysts and PID [7], and the female infertility is the most common symptom, especially in developing countries [8] Furthermore, genital TB plays an important role in the establishment of EP [9]. Combined with the patient medical history, she may experience a tubal pregnancy. Then the ectopic gestation happens to rupture in first trimester and the embryo continues to grow and develop in the fallopian tube and ovary. . On the other hand, we also have found three possible explanations to the implantation site in ovary. 1) The extrauterine fetus had been developed as 13 weeks gestation, and rich blood supply is an essential precondition. Only the ovary but not the tubal can offer the rich blood supply. 2) When the late blastocyst embed, trophoblastic cells start proliferating and forming chorion frondosum, which is the main structure of the placenta, and in the case, just the ovary with fresh placenta attached. 3) As Shan

et al.[10] suggested that various abdominal surgeries could change the inherent structure of the uterus and may result in ovarian inflammation, ovulation barriers and fertilized eggs implanted in the ovary. But, how the fetal tissue got to the tubal? We can not relate the phenomena with any theory we have known.

The incidence of HP comprising up to 1%-3% of all EP in the IVF - ET settings [2,3], resulting from the increasing number of PID, more frequent performance of surgery in the pelvic and the increasing usage of ART. As Jeon *et al* . [10] noted, previous ectopic pregnancy (EP), abortion, and ovarian hyperstimulation syndrome (OHSS) may be significant risk factors for subsequent HP in patients following IVF - ET. In addition, early report shown that the incidence of HP in ART settings had an association with a multiple embryo transplant [11]. Shortly, some researchers took the contrary opinion [12]. More studies are needed to detect such an effect. Meanwhile, it may be better to minimize the embryo transfer number or transfer single embryo.

Furthermore, our patient had attended in different two hospitals, and the ultrasound follow - up were variable, easily led to mislead in clinical diagnosis or treatment. As Li *et al* . [13] stated that the early regular ultrasound monitoring, the clinical experience and the ultrasonic level of sonologist were all the essential preconditions in the correct diagnosis among women following ART. In recent years, laparoscopy is accepted as the gold standard of treatment [14], especially for the intrauterine - tubal pregnancy [15]. After active treatment, positive tocolyis and dynamic monitoring, term delivery of intrauterine pregnancy reached 65% [1].

To conclude, the diagnosis of proven HP is challenging and easily misdiagnosed. For this reason early recognition of HP following ART is of importance in order to prevent a fatal event through urgent laparoscopy. Physicians involved should not only pay attention to the intrauterine pregnancy, especially for IVF - ET patients with high risk factors of ectopic pregnancy and transfer more than one embryo at the same time. And ultrasonic monitoring time should be extend not only confined to 2 months after transplantation.

Declaration of Conflicting Interests

The author(s) declared no conflict of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval and consent to participate

This respective study was approved by the Research and Ethical Committee of the Second Hospital of Hebei Medical University, China, basing on the 1964 Helsinki declaration and its later amendments.Additional informed consent was obtained from the patient for which identifying information is included in this article.

Author Contribution

WW, JHZ and XSZ had designed the research. JHZ and XSZ drafted the manuscript. JHZ, XSZ, XJZ, and LLW collected and made all the figures and in this manuscript. WW had guided the writing. All authors read and approved the final manuscript.

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