



## Case Report

# A Rare Heterotopic Pregnancy Following Frozen Embryo Transfer: A Diagnostic and Therapeutic Challenge

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## ABSTRACT

Ectopic pregnancy is a common obstetric emergency, occurring in approximately 2–3% of pregnancies. Heterotopic pregnancy, defined as the coexistence of intrauterine and ectopic gestations, is rare but increasingly encountered with the widespread use of assisted reproductive technologies, accounting for nearly 1% of in vitro fertilisation (IVF) pregnancies. Early diagnosis remains challenging, particularly in IVF patients, where ovarian hyperstimulation–related ascites may obscure clinical and ultrasonographic findings. We report a case of a 32-year-old woman with primary infertility who conceived following IVF and frozen embryo transfer and presented with mild abdominal pain and vaginal bleeding after a positive pregnancy test. Ultrasonography revealed twin intrauterine gestations with a concomitant ruptured right tubal ectopic pregnancy and free intraperitoneal fluid. Emergency laparoscopic evaluation confirmed a ruptured right ampullary ectopic pregnancy, and laparoscopic salpingectomy was successfully performed. The patient had an uneventful postoperative recovery and was discharged on postoperative day one. The intrauterine twin pregnancy progressed without complications, and at 36 weeks of gestation, an emergency caesarean section was performed for premature rupture of membranes with breech presentation of both fetuses, resulting in the delivery of healthy male and female neonates. This case highlights that heterotopic pregnancy should be considered even in the presence of a confirmed intrauterine gestation, particularly following assisted reproductive techniques. Early transvaginal ultrasonography by experienced clinicians is essential for timely diagnosis, and laparoscopic management of the ectopic component is a safe and effective treatment option that can preserve the ongoing intrauterine pregnancy and achieve favourable maternal and perinatal outcomes.

**Keywords:** Assisted reproductive technology; Frozen embryo transfer; Heterotopic pregnancy; Laparoscopic salpingectomy; Twin pregnancy

## INTRODUCTION

Ectopic pregnancy is among the most common causes of acute abdominal emergencies in obstetrics and gynaecology, with an incidence of ~2–3%.<sup>[1]</sup> Heterotopic pregnancy refers to the simultaneous presence of an intrauterine pregnancy along with an ectopic pregnancy, and its incidence has been rising, particularly in assisted reproductive techniques, accounting for approximately 1% of *in vitro* fertilisation (IVF) pregnancies.<sup>[2]</sup> Early confirmation of this diagnosis remains challenging for clinicians, as the presence of an intrauterine pregnancy often leads to ectopic pregnancy being overlooked in routine practice; consequently, diagnosis may be delayed until significant internal bleeding occurs due to rupture of the ectopic gestational sac.<sup>[3]</sup> Moreover, in IVF patients, ascites caused by ovarian hyperstimulation can closely mimic

intraperitoneal bleeding, making differentiation from internal haemorrhage particularly difficult.<sup>[4]</sup>

## CASE REPORT

A 32-year-old woman presented to our clinic with infertility. She had been married for 10 years. She underwent evaluation, and her Anti-Müllerian hormone (AMH) level was 3.1 ng/mL. Her remaining hormonal parameters were within normal limits. Her husband's semen analysis was also within normal limits. Then she was planned for IVF. She was stimulated with Inj. Gonal-f 225 subcutaneous (follicle-stimulating hormone injection - Merck Serono S.p.A., Italy) from day 2 of the cycle and Inj. Gonapress (antagonist) subcutaneous (cetorelix acetate 0.25mg - Ferring Pharmaceuticals) was added from day 7 as part of a flexible antagonist protocol. From day 8, Inj. Menotas 300IU subcutaneous (menotropin injection - INTAS Pharmaceuticals Ltd.) was added along with the antagonist until the day of trigger. Final oocyte maturation was achieved with Inj. Ovitrelle 250mcg subcutaneous (choriogonadotropin alfa - r - DNA Human Chorionic Gonadotropin (hCG) - Merck). A total of 10 oocytes were retrieved on the day of ovum pick-up, and 8 Grade-A day-3 embryos, as per the Indian Society for Assisted Reproduction (ISAR) Consensus Guidelines (2019-2021), were cryopreserved. In the subsequent cycle, the endometrium was prepared using a modified natural cycle, and 3 frozen embryos were transferred on the scheduled day of embryo transfer. After 15 days of embryo transfer, her Serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) was positive, with a  $\beta$ -hCG level of 1252.1mIU/mL. After 7 days of positive BHCG, she presented with mild abdominal pain on the right side and mild bleeding per vaginum. Her vital signs showed a heart rate of 101 bpm and blood pressure of 96/68 mmHg. Her haemoglobin was 12.1 g/dL. Ultrasonography has uncovered free fluid in the cul-de-sac, twin intrauterine gestational sac [Figure 1], and rupture of the right ectopic pregnancy [Figure 2]. Under the impression of internal bleeding, she was taken for emergency laparoscopy. On diagnostic laparoscopy, we found a ruptured ectopic (ampullary) pregnancy on the right side, and minimal haemorrhagic fluid was present in the pouch of Douglas. So we decided to do a right salpingectomy. Correspondingly, the left side adnexa was normal. The abdomen was cleared entirely with saline solution. To support intrauterine pregnancy, oral and intramuscular progesterone injections were given for luteal support, and a single shot of antibiotic intravenous (IV) (ceftriaxone 1gm - ARISTO Pharmaceutical Private Ltd.) was given. No analgesic was given; only a paracetamol suppository (Neomol 250 - per rectum) (NEON Laboratories Limited) was given as per requirement. After 24 hours, the patient was stable and was discharged. After 7 days, the twin intrauterine (DCDA) pregnancies were confirmed again on ultrasound. Her antenatal period was uneventful. At

36 weeks of gestation, the patient presented with premature rupture of membranes, and in view of breech presentation of both foetuses, an emergency cesarean section was performed, resulting in the delivery of twins (one male and one female) without any antenatal or postnatal complications.



**Figure 1:** Intra-uterine twin pregnancy - Transvaginal ultrasonography (TVS) showing an intrauterine twin pregnancy with two gestational sacs corresponding to 5 weeks and 5 days of gestation.



**Figure 2:** Right ectopic pregnancy - Transvaginal ultrasonography (TVS) showing a right tubal ectopic pregnancy.

## DISCUSSION

Ectopic pregnancy can be managed using a variety of treatment approaches, depending on the clinical presentation and patient factors.<sup>[5]</sup> Non-surgical management options for ectopic pregnancy include local or systemic methotrexate administration, and in selected cases, local potassium chloride injection with or without adjunctive systemic methotrexate; however, in the setting of heterotopic pregnancy, methotrexate

is contraindicated because of its toxic effects on the coexisting intrauterine pregnancy.<sup>[6]</sup> Although local injection of potassium chloride or hyperosmolar glucose can be effective, these methods may leave persistent trophoblastic tissue in situ throughout the course of the ongoing intrauterine pregnancy; therefore, surgical removal of the ectopic gestational sac is generally preferred. However, there is no clear consensus on whether laparoscopy or laparotomy is the optimal surgical approach, and Vilos reported a case of heterotopic pregnancy managed laparoscopically that was followed by growth restriction of the surviving intrauterine pregnancy.<sup>[7]</sup> Recent review articles and case series have increasingly demonstrated that laparoscopy can be performed safely during pregnancy.<sup>[4,8]</sup> In our case, laparoscopic salpingectomy was uneventful, and the patient was discharged one day after surgery with no associated maternal or perinatal complications.

## CONCLUSION

The incidence of heterotopic pregnancy is increasing due to the widespread use of assisted reproductive technology. An early transvaginal sonography performed by an experienced radiologist/radiographer is considered to be essential and beneficial in establishing early diagnosis of heterotopic pregnancy. Both salpingectomy and selective fetal reduction by embryo aspiration can be administered as one of the effective therapies for heterotopic pregnancy, with the optimal outcome of intrauterine pregnancy. Choice of surgical intervention for heterotopic pregnancy depends on the clinician's surgical expertise as well as the patient's socioeconomic situation. Laparoscopic surgery is a safe and effective treatment, and most patients can achieve satisfactory pregnancy outcomes after surgery.

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