

Case Study

From Silent to Acute: Contrasting Presentations of Heterotopic Pregnancy following Assisted Reproduction

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Abstract - Heterotopic Pregnancy (HP), the coexistence of intrauterine and ectopic gestation, is a rare but increasingly encountered condition with the rise in Assisted Reproductive Techniques (ART). Early diagnosis remains challenging due to the presence of a concurrent intrauterine pregnancy, often leading to delayed recognition. We present two cases of heterotopic pregnancy with contrasting clinical presentations. The first case involved a 31-year-old G2P1L1 with ovulation induction conception presenting with minimal spotting and no abdominal pain. Ultrasound demonstrated a viable intrauterine pregnancy with a concurrent unruptured left tubal ectopic pregnancy. She underwent timely laparoscopic salpingectomy, with continuation of intrauterine pregnancy to term, resulting in a live birth. The second case involved a 30-year-old primigravida with ICSI conception presenting at 7+ weeks with acute abdominal pain and spotting per vaginum. Ultrasound revealed a viable intrauterine pregnancy along with a right adnexal mass and significant hemoperitoneum, suggestive of a ruptured ectopic pregnancy. Emergency laparoscopy confirmed the diagnosis, and salpingectomy was performed. These cases highlight the varied clinical spectrum of heterotopic pregnancy, ranging from asymptomatic to life-threatening presentations. Risk factors such as ART and ovulation induction necessitate a high index of suspicion. Transvaginal ultrasound plays a pivotal role in early diagnosis. Early recognition and prompt surgical management are crucial to prevent morbidity while preserving the intrauterine pregnancy. Clinicians must remain vigilant in high-risk patients to ensure favourable maternal and fetal outcomes.

Keywords - Heterotopic pregnancy, Assisted reproductive techniques, Tubal ectopic pregnancy, Laparoscopy, Case series.

1. Introduction

Heterotopic pregnancy refers to the simultaneous occurrence of intrauterine and ectopic pregnancies, irrespective of the ectopic implantation site. The fallopian tube is the most common site of ectopic pregnancy(1). Other sites being, the cornua and in rare instances occur at caesarean section scar sites, the ovary, abdominal cavity and cervix (2). The incidence of heterotopic pregnancy is estimated to be 1 in 30,000 in spontaneous conception and 1 in 100 with the use of Assisted Reproductive Techniques (ART), including intrauterine insemination (IUI), super ovulation and in vitro fertilization (IVF). According to more recent literature, clomiphene citrate could be related to a higher incidence of heterotopic pregnancy as it increases the rate of twinning(3). Assisted reproduction has transformed a 0.003% rarity into a 1% reality.

Clinical symptoms include abdominal pain, adnexal mass, signs of peritoneal irritation and an enlarged uterus. Unlike isolated ectopic pregnancy, vaginal bleeding is an uncommon presentation in heterotopic pregnancy. Heterotopic pregnancy can result in severe and potentially fatal complications, including intra-abdominal bleeding, uterine rupture, preterm delivery or miscarriage (4). The

main aim of treating such pregnancies is to remove the ectopic pregnancy, while maintaining the normal intrauterine pregnancy, so as to decrease the risk of adverse pregnancy outcomes(5).

Diagnosis is often challenging, with most cases identified between 5 and 10 weeks of gestation. Physical examination and TVS play a major role in diagnosis. Ultrasonographic features include the presence of an intrauterine gestational sac associated with heterogenous adnexal mass corresponding to hematosalpinx or the visualization of the extra-uterine mass surrounded by an echogenic trophoblastic halo, sometimes with an embryo. The presence of hemoperitoneum supports the diagnosis(6). Serum β -hCG is not reliable in these pregnancies. We report two contrasting presentations of heterotopic pregnancies to highlight its variable clinical spectrum and to emphasize the diagnostic challenges despite the presence of an intrauterine pregnancy. And how timely management improves maternal and fetal outcomes.

2. Case Series

Here we have a clinical contrast. Case 1, a silent threat and Case 2, an acute emergency.



2.1. Case-1: Silent Presentation with Unruptured Tubal Ectopic Pregnancy

A 31-year-old, G2P1L1 at 7+5 weeks of gestation, previous LSCS, conceived with ovulation induction, presented with a complaint of spotting per vaginum. The patient was hemodynamically stable at presentation. Her initial serum β -hCG was 774.

Transvaginal scan revealed a single live intrauterine gestational sac of 7+3 weeks gestation, CRL corresponding to 7+1 weeks with fetal heart rate of 156 bpm. On subsequent adnexal screening, left tubal ectopic pregnancy with Gestational sac of 12 mm and with CRL corresponding to 6+5 weeks gestation and fetal heart rate of 130 bpm was noted. There was no free fluid in POD. Careful adnexal evaluation was essential, as premature termination of the scan after identifying the intrauterine pregnancy could have resulted in a missed diagnosis. A diagnosis of heterotopic pregnancy was established, consisting of a viable intrauterine pregnancy with a concurrent unruptured left tubal ectopic pregnancy.

After counselling, an emergency laparoscopy was performed. Intraoperatively, there was left unruptured tubal ectopic pregnancy was noted (Figure 1) and left salpingectomy was performed without disturbing the uterus or the intrauterine pregnancy. The contralateral fallopian tube appeared normal. The intra-operative and post-operative period were uneventful. Patient was discharged home on post-operative day 2. She was put on progesterone supplements to support her intrauterine pregnancy. She

continued her pregnancy till term and delivered a live, term, female baby via caesarean section.

2.2. Case-2: Acute Presentation with Ruptured Tubal Ectopic Pregnancy

30 years, Primigravida 7+3 weeks with ICSI conception, presented with complaints of lower abdominal pain and spotting p/v. She has a past surgical history of a laparoscopic cholecystectomy done 3 years back. Frozen embryo transfer was done, and her initial serum β -hCG was 1215.

TVS was done, and it showed a single live intrauterine gestation with CRL corresponding to 7+3 weeks of gestation and a fetal heart rate of 166 bpm. On subsequent adnexal screening, there was a right adnexal mass measuring 3.7 x 2.9 cms with significant free fluid in POD. Emergency laparoscopy was performed in view of suspected heterotopic pregnancy and to exclude other causes of acute abdomen in pregnancy.

Intraoperatively, there was moderate hemoperitoneum (Figure 2), and there was a ruptured right tubal ectopic pregnancy (Figure 3). Right salpingectomy was performed, and the hemoperitoneum was suctioned without uterine manipulation and without disturbing the intrauterine pregnancy. Post operative period was uneventful. Patient was discharged on post-operative day 2. Patient was given progesterone supplements to support her intrauterine pregnancy. The intrauterine pregnancy has remained uneventful on follow-up.

3. Summary of Cases

Table 1. Comparison of clinical features, management, and outcomes. FHR, fetal heart rate; LSCS, lower-segment caesarean section; TVS, transvaginal ultrasonography

Feature	Case 1	Case 2
Maternal profile	31 years; G2P1L1; prior LSCS	30 years; primigravida; prior laparoscopic cholecystectomy
Conception	Ovulation induction	ICSI conception; frozen embryo transfer
Gestation at presentation	7+5 weeks	7+3 weeks
Presenting symptoms	Spotting per vaginam; haemodynamically stable	Lower abdominal pain and spotting per vaginam
TVS: intrauterine pregnancy	Live; 7+3 weeks; CRL 7+1 weeks; FHR 156 beats/min	Live; CRL 7+3 weeks; FHR 166 beats/min
TVS: ectopic component	Left tubal sac, 12 mm; CRL 6+5 weeks; FHR 130 beats/min; no free fluid	Right adnexal mass, 3.7 × 2.9 cm; significant free fluid
Operative finding	Unruptured left tubal ectopic pregnancy	Ruptured right tubal ectopic pregnancy with moderate haemoperitoneum
Management	Emergency laparoscopy and left salpingectomy	Emergency laparoscopy, right salpingectomy, and suction of haemoperitoneum
Maternal outcome	Uneventful recovery; discharged postoperative day 2	Uneventful recovery; discharged postoperative day 2
Intrauterine pregnancy outcome	Continued to term; live term female infant delivered by caesarean section	Uneventful on follow-up (final outcome not reported in the supplied record)

Early pregnancy assessment

Confirm symptoms, haemodynamic status, conception method, and risk factors (ART, prior ectopic pregnancy, tubal disease/surgery, pelvic inflammatory disease, endometriosis).

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Perform transvaginal ultrasonography

Assess the uterus and systematically examine both adnexa and the pouch of Douglas, irrespective of whether an intrauterine pregnancy is seen.

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Intrauterine pregnancy identified

Do not end the scan at confirmation of the intrauterine gestation. Continue bilateral adnexal assessment and assess for free fluid.

↓

Adnexal mass / extrauterine sac / free fluid present

Consider heterotopic pregnancy. Urgently involve senior obstetrics–gynaecology and ultrasound teams; assess for rupture and haemodynamic compromise.

↓

Haemodynamic instability, peritoneal signs, or suspected rupture

Resuscitate and proceed to urgent operative management according to local protocol. Minimise uterine manipulation where preservation of the intrauterine pregnancy is intended.

↓

Stable patient with suspected or confirmed unruptured ectopic component

Individualise management (surgical, selected local treatment, or carefully monitored expectant management) after multidisciplinary counselling; ensure clear safety-netting and follow-up.

4. Suggested Diagnostic Algorithm for Suspected Heterotopic Pregnancy

This practical algorithm is based on the diagnostic principles described in the cited literature and is intended to support, not replace, local emergency and ultrasound protocols.

Box 1. Suggested diagnostic algorithm. Serum β -hCG alone is not reliable for diagnosing heterotopic pregnancy because the intrauterine pregnancy may mask expected ectopic pregnancy trends [1,4,6].

5. Discussion

Heterotopic pregnancy is defined as the coexistence of an ectopic and intrauterine pregnancy. The important risk factors for heterotopic pregnancy include unnoticed chronic Chlamydia trachomatis infections, previous ectopic pregnancy, tubo-ovarian abscess, previous tubal surgery, tubal disease, endometriosis, history of pelvic inflammation, high hormone levels and embryo transfer techniques. The diagnosis of heterotopic pregnancy remains challenging, particularly in the presence of a confirmed intrauterine gestation. It is often delayed due to the early visualization of an intrauterine sac with late detection of adnexal abnormalities (1). Multiple embryo transfers in ART techniques are also associated with a high risk of heterotopic pregnancies(6). The direct insertion of the embryos into the utero-tubal orifice has been previously suggested as one explanation. Another theory is, migration of embryos from the uterus into the tube, mediated by the female genital tract itself. Carbon particles can be identified in the fallopian tube shortly after their deposition in the vagina. This finding also suggests an inherent retrograde mechanism for transfer of nonmotile particles. Dimitry et al found that tubal disease

was the main cause of infertility in all the nine cases of heterotopic pregnancy reported by him(7). Lyu et al. advises to perform transvaginal scan in every woman after in vitro fertilization, 4 weeks following embryo transfer(8).

The distance from the tip of transfer catheter to uterine fundus has also been evaluated as a potential risk factor for development of heterotopic pregnancy in the study conducted by Zhu et al, distance of air bubble to fundus was controlled in 15–20 mm range, and the data suggested no significant difference between heterotopic and intrauterine pregnancy (17.55 ± 1.80 vs. 17.32 ± 1.75 mm, $p = 0.55$). The result was consistent with a study by Fiçicioglu et al., which reported that air bubble position too close to the fundus (10 mm) probably ended in a tubal pregnancy, while at a distance of 15–20 mm would achieve a higher rate of embryo implantation(9).

The diagnosis of heterotopic pregnancy remains one of the greatest challenges of the gynecological emergencies. It is often delayed due to the early visualization of an intrauterine sac, with late detection of adnexal abnormalities. Clinical symptoms may mimic threatened abortion. The most common symptoms include abdominal pain, vaginal bleeding, peritoneal irritation and uterine enlargement. These symptoms can be misleading when we had isolated abdominal pain associated with an intrauterine pregnancy. Delayed diagnosis may result in tubal rupture, massive hemoperitoneum, and maternal hemodynamic instability(6).

Case report by Cherkaoui et al revealed a bi-foetal, bi-chorionic, and bi-amniotic intrauterine pregnancy, as well as a third gestational sac lateralized to the left, which appeared to be outside the uterine cavity, containing a foetus

with an estimated gestational age of 13 weeks, whose placenta was separate from the others. The pregnancy was progressing well, with 3 fetuses having positive cardiac activity and good morphological development. An additional MRI was performed in an emergency setting. It clearly showed the third gestational sac in the abdominal cavity adjacent to the uterus, not surrounded by myometrium, containing a fetus and placenta of its own. In such an abdominal pregnancy, the blood supply is provided by the omentum or an intra-abdominal organ (10).

70% of heterotopic pregnancies are diagnosed between 5 and 8 weeks. Transvaginal ultrasonography remains the cornerstone of diagnosis(4). Intrauterine pregnancy with hemorrhagic corpus luteum can simulate heterotopic pregnancy or ectopic gestation, both clinically and on sonography. Bicornuate uterus with gestation in both horns also mimic a heterotopic pregnancy. Taylor and coworkers have described a high-resolution transvaginal ultrasonography with color Doppler will be helpful, as the trophoblastic tissue in the case of heterotopic pregnancy shows increased flow with significantly reduced resistance index is an important aid in the diagnosis of heterotopic pregnancy(11).

Lugata et al reported a case of spontaneous conception of heterotopic pregnancy, in which the ectopic was a ruptured right cornual pregnancy and a intrauterine pregnancy corresponding to 18 weeks of gestation. Laparotomy was done and found to have a ruptured right cornual pregnancy extending to the isthmus with a floating fetus. Wedge resection of the right cornu-isthmic portion of the tube was done. Patient was kept on tocolytics for one week. The intrauterine continued till term and was delivered via caesarean section (12). Due to the ongoing development of intrauterine pregnancies, cornual resection may increase the risk of uterine rupture during pregnancy due to its impact on uterine integrity. Therefore, Cornuostomy is preferred over cornual resection. In the study conducted by Ma et al, patients with interstitial tubal and cornual pregnancies underwent Cornuostomy to remove the gestational tissue, followed by continuous closure of the wound using 1–0 absorbable sutures(2).

Serum β -hCG level is not useful for diagnosing heterotopic pregnancy. Intrauterine pregnancy masks all underlying β -hCG changes from ectopic pregnancy and vice versa. Management may be medical or surgical, depending on clinical stability, and early intervention is crucial for optimal outcomes. Aim is to conserve the intrauterine gestation, while removing the ectopic pregnancy, preserve the patient's fertility and avoid recurrence. For asymptomatic or hemodynamically stable patients, expectant management can be suggested in order to avoid surgery and transvaginal ultrasound-guided aspiration's complications. In case of hemodynamic instability, with signs of the ectopic being ruptured, emergency surgery is highly recommended. Surgery mainly involves either a salpingectomy, salpingotomy or oophorectomy. In some difficult cases, it may also require a hysterectomy. Minimal

uterine manipulation is essential to preserve the intrauterine pregnancy. Laparotomy is indicated in cases of hemodynamic instability or large hemoperitoneum(1).

Laparoscopic approach provides a broad field of view, reduces surgical time, minimizes uterine stimulation from open surgery, lowers the risk of postoperative miscarriage in intrauterine pregnancies, and promotes faster patient recovery. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) recommends strict control of intra-abdominal pressure <12 mmHg and surgery performed by experienced laparoscopic surgeons for patients requiring continued intrauterine pregnancies to reduce surgical duration and carbon dioxide abdominal damage. During surgery, efforts are made to select anaesthetics that are non-teratogenic to the fetus, avoid the use of monopolar electrocautery to prevent current backflow affecting the intrauterine fetus, and aim to expel as much carbon dioxide from the abdominal cavity post-surgery(2).

For asymptomatic, hemodynamically stable patients and no evolutive ectopic pregnancy, expectant management can be suggested. Intramuscular injection of Methotrexate may be an alternative only if the intrauterine pregnancy is not progressive(6). Medical treatment, i.e. potassium chloride or hyperosmolar glucose, has to be injected locally to the intact heterotopic gestational sac or fetus via laparoscopy or TVS(13).

Prognosis of ectopic pregnancies were better if it were in the ampulla of fallopian tube. Smaller size and ampulla located pregnancy involves a simpler surgical procedure and shorter duration of operation (salpingectomy), less manipulation of the uterus and surgical complications, which was a key point for a better reproductive outcome(9). Progestin therapy can be used to avoid post-operative abortion. A 800 mg of Micronized progesterone was administered to four patients with intrauterine active pregnancies in the case report published by Lamrissi et al(6).

Future prospective, multicentre registries should standardise reporting of conception method, number and type of embryos transferred, ultrasound findings, ectopic location, treatment, maternal morbidity, and intrauterine pregnancy outcomes. Comparative studies are needed to define selection criteria and outcomes for laparoscopy, expectant management, and local treatment in stable patients. Research should also evaluate the diagnostic performance and implementation of standardised bilateral-adnexal scanning protocols after ART, as well as patient-centred outcomes and longer-term reproductive outcomes after conservative versus radical tubal surgery.

6. Conclusion

The presence of an intrauterine pregnancy does not exclude a concurrent ectopic pregnancy. Never allow a healthy intrauterine pregnancy to provide a false sense of security. Maintain a high index of suspicion. Clinicians should maintain a high index of suspicion for heterotopic

pregnancy in patients conceived through assisted reproductive techniques. Systematic bilateral adnexal evaluation should be performed in all early pregnancy scans, particularly following assisted reproduction. Make bilateral adnexal evaluation a non-negotiable standard, regardless of presenting symptoms or intrauterine pregnancy confirmation.

Ethical Statement

Written informed consent was obtained from both patients for publication of clinical details and images. Patient anonymity has been maintained.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Figures

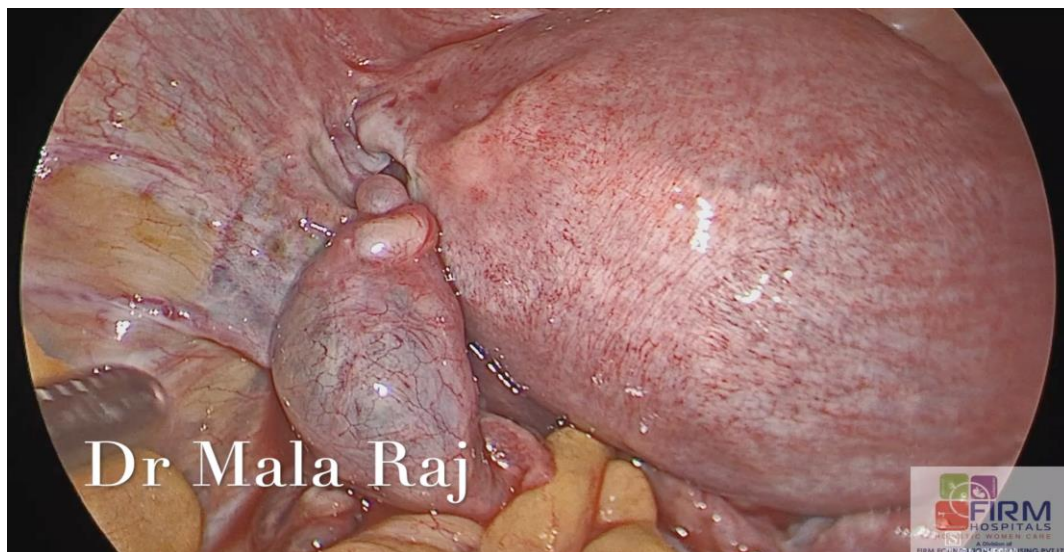


Fig. 1 Left unruptured tubal ectopic pregnancy with a live intrauterine gestation

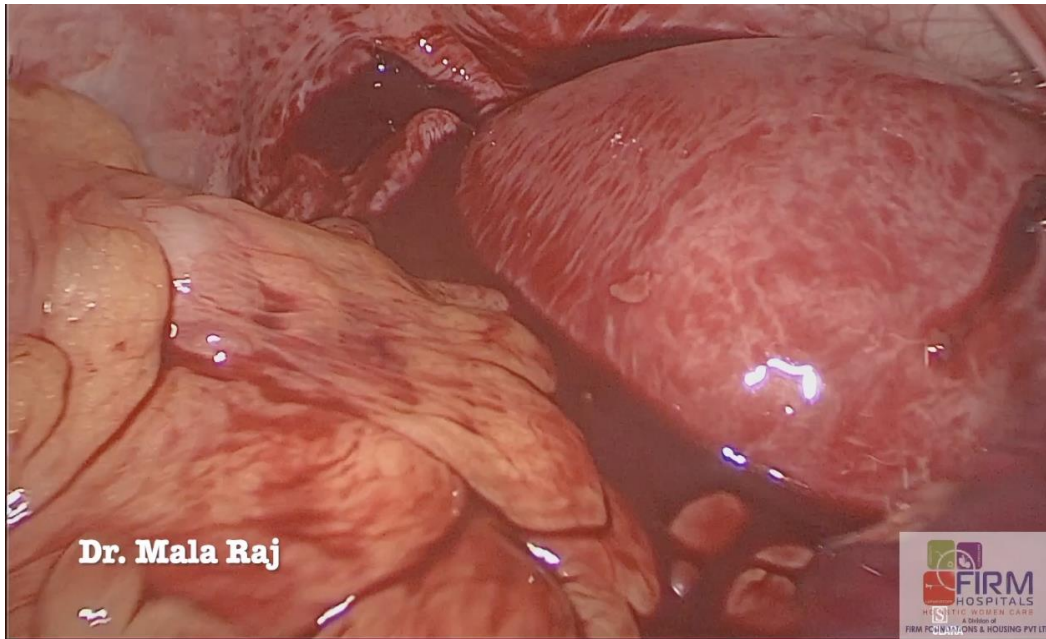


Fig. 2 Hemoperitoneum due to ruptured tubal ectopic pregnancy

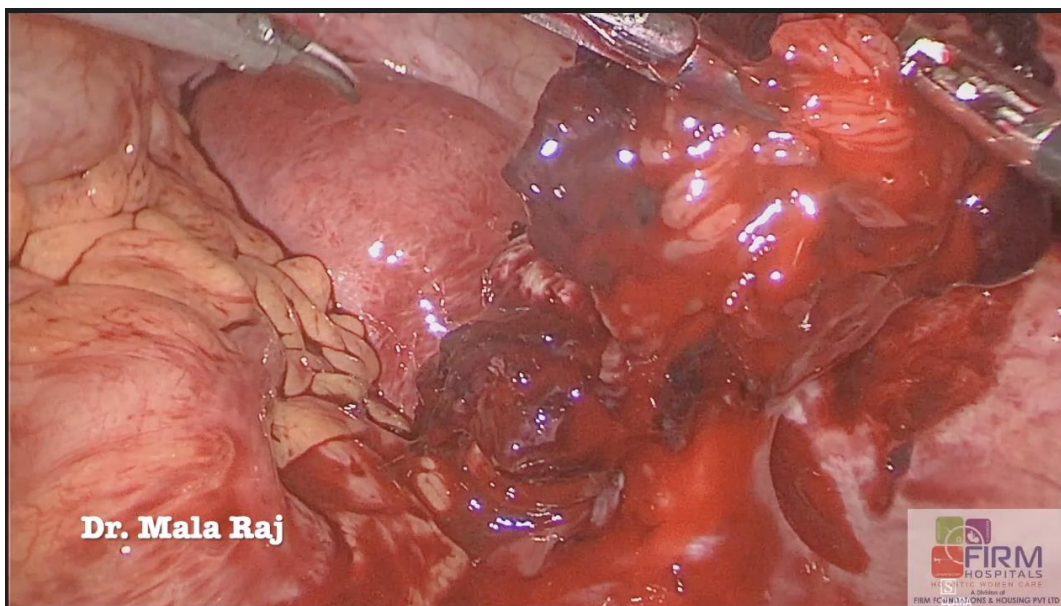


Fig. 3 Evidence of right ruptured tubal ectopic pregnancy with a live intrauterine gestation