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Abdominal heterotopic pregnancy post-IVF double embryo transfer

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SUMMARY

Uterosacral ligament (USL) is an uncommon site of implantation for abdominal ectopic pregnancies. This is the first case of USL heterotopic pregnancy post invitro fertilisation (IVF). The patient presented 6 weeks after a double embryo transfer with acute onset abdominal pain and was diagnosed with a suspected live tubal ectopic pregnancy with a viable intrauterine pregnancy on ultrasound. A diagnostic laparoscopy revealed an ectopic pregnancy implanted on the left USL which was resected and confirmed on histology. The patient was discharged well on postoperative day 2 with a viable intrauterine pregnancy. This case highlights the importance of considering non-tubal heterotopic pregnancies in the context of risk factors including IVF with double embryo transfer presenting with abdominal pain.

BACKGROUND

Heterotopic pregnancies in the general population are rare, occurring 1 in 3889 to 1 in 30000 pregnancies.¹ The incidence increases among invitro fertilisation (IVF) patients, occurring approximately 1 in 100 to 1 in 1000 IVF pregnancies.²⁻⁴ There is a correlation between the number of embryos transferred and the risk of ectopic pregnancy.⁴⁻⁶ Fresh embryo transfer (ET) cycles have also been shown to increase the risk of heterotopic pregnancies post-IVF ET compared with frozen ET cycles.⁷ Other risk factors for heterotopic pregnancies include abnormal tubal anatomy due to previous tubal ectopic pregnancy, previous tubal surgery and endometriosis.⁸ The most common location for

heterotopic pregnancies was tubal, accounting for almost 90% of cases.⁹ 10.8%–11.8% of heterotopic pregnancies implant at non-tubal sites, and 1.3%–2.7% are abdominal.^{6 10 11}

In this case report, we present a case of abdominal heterotopic pregnancy implanted in the uterosacral ligament (USL) after double frozen ET.

CASE PRESENTATION

The patient is a primigravida in her 30s who presented 6 weeks post-ET with a 1 day history of sudden onset, sharp, colicky abdominal pain associated with nausea and non-bloody, non-bilious vomiting, and two episodes of diarrhoea. She had no vaginal bleeding and no contact with sick patients. On physical examination, she was alert, afebrile and had a heart rate of 90 beats per minute, but was hypotensive with blood pressure of 84/54 mm Hg. Her abdomen was soft with mild tenderness in the left iliac fossa with no rebound tenderness or guarding. On speculum examination, the cervical os was closed with no per vaginal bleeding or discharge.

She had a history of unexplained primary subfertility. The patient underwent hysterosalpingo-foam sonography which showed patency of both tubes, and normal endometrial cavity with no endometrial polyps or submucosal lesions. However, there were multiple intramural fibroids seen, ranging in size from 0.8 to 4.3×3.1×3.4 cm. She underwent an antagonist cycle with recombinant follicle-stimulating hormone 225 IU/L and gonadotropin-releasing hormone antagonist 0.25 mg. Eighteen eggs and eventually six blastocysts were obtained. Fresh transfer of one blastocyst was unsuccessful; hence, she went on to transfer two blastocysts on the frozen cycle. Two weeks later, her beta-human chorionic gonadotropin (β-hCG) level was 4682.3 mIU/mL. The review 4 weeks post-ET showed an intrauterine gestational sac (IUGS) and yolk sac with crown-rump length of 7 mm (corresponding to approximately 6 weeks' gestation) and positive foetal heart on ultrasound. There was no adnexal mass seen on the scan, and she was asymptomatic at that point in time.

INVESTIGATIONS

Bedside transvaginal ultrasound (TVUS) showed a viable intrauterine pregnancy (IUP) with a live ectopic seen in the left adnexa. The findings were suspicious for a heterotopic pregnancy. A second diagnostic TVUS performed in the radiology department confirmed the suspected diagnosis of heterotopic pregnancy with a live extrauterine pregnancy



Figure 1 Ultrasound scan showing a heterotopic pregnancy. (A) Transabdominal and (B) transvaginal ultrasound showing both intrauterine and ectopic pregnancy. (C) Left adnexal mass corresponding to likely tubal ectopic pregnancy. (D) Size of foetal pole corresponding to crown-rump length 1.8 cm. (E) Live ectopic pregnancy with positive foetal cardiac activity.



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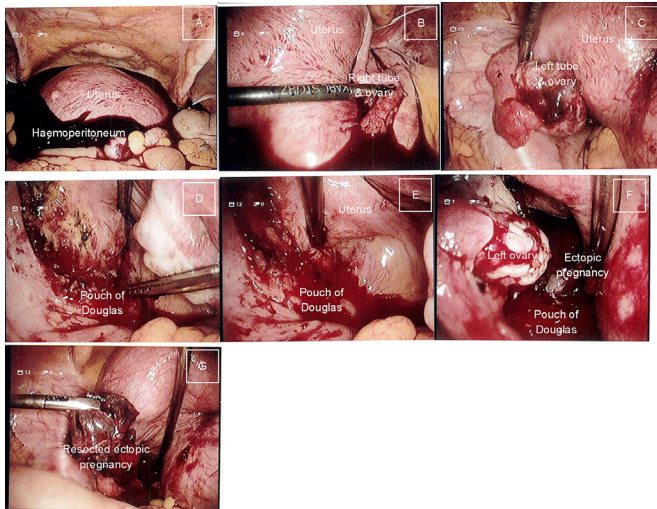


Figure 2 Resection of uterosacral ligament ectopic pregnancy. (A) Haemoperitoneum seen on entry into abdomen. (B) Normal right tube and ovary. (C) Normal left tube and ovary. (D–F): Mass with bleeding in pouch of Douglas. (G) Resected ectopic pregnancy from left uterosacral ligament.

corresponding to 8.3 weeks' gestation (figure 1). There was also a viable IUP seen corresponding to 8.9 weeks' gestation. There were also two uterine fibroids which measured 5.6×5.3×4.9 cm and 2.9 cm. There was no free fluid in the pouch of Douglas, but a heterogeneous mass was seen around the ectopic pregnancy suspected to be a blood clot.

The initial haemoglobin level was 95 g/L. A group and cross-match for two units of blood was also performed.

TREATMENT

The patient underwent a diagnostic four-port laparoscopy for a suspected left tubal ectopic pregnancy. Intraoperative findings showed a uterus of 10 weeks' size and multiple fibroids. Haemoperitoneum was noted on entry, suspicious of a ruptured ectopic pregnancy (figure 2A). However, both tubes were normal with no ectopic pregnancy seen, and ovaries were also normal bilaterally (figure 2B,C). Clots were evacuated and the pouch of Douglas was explored. Fresh bleeding was noted over the left USL with suspected products of conception (POC) (figure 2D–F). The ureter was identified and the POC were carefully dissected off the left USL (figure 2G). The specimen was retrieved in a bag and sent for histology. Interrupted sutures were applied, and topical haemostatic agents, including oxidised regenerated cellulose and human gelatine-thrombin matrix sealant, were applied over the left USL to secure haemostasis. An adhesion barrier was applied. The abdomen was then desufflated and the umbilical port closed with braided absorbable sutures. Two units of packed cells were transfused intraoperatively. The estimated blood loss was 2000 mL. A bedside transabdominal ultrasound done immediately postoperatively confirmed a viable IUP.

OUTCOME AND FOLLOW-UP

The patient remained haemodynamically stable in the ward with a haemoglobin level of 103 g/L on postoperative day 1 and was discharged well on the second postoperative day. Ultrasound for viability prior to discharge confirmed that the IUP was still viable. She was given a single dose of intramuscular progesterone 100 mg and kept on oral progestogen 10 mg two times per day. Histopathological findings of the resected specimen confirmed

POC, with vascularised chorionic villi seen. She was last seen in the clinic on 12 July 2021 with a viable IUP and a low-risk Down syndrome screening result.

DISCUSSION

Abdominal heterotopic pregnancies are rare occurrences with few cases reported. Here we present a case of a primigravida in her 30s with a history of unexplained subfertility who had an abdominal heterotopic pregnancy post-IVF double ET. She presented with acute onset abdominal pain and hypotension. A heterotopic tubal pregnancy was initially suspected on ultrasound imaging. The diagnostic laparoscopy revealed an abdominal heterotopic pregnancy implanted on the left USL, which was surgically resected. The patient was discharged well with a viable IUP.

Heterotopic pregnancies present an interesting diagnostic and therapeutic dilemma. Herein, we aim to present contemporary evidence-based management of heterotopic pregnancies, with particular focus on abdominal heterotopic pregnancies (figure 3).

Diagnosis

Diagnosis of a non-tubal heterotopic pregnancy can be challenging as both presentation and ultrasound findings are similar to tubal heterotopic pregnancies.¹² Patients with heterotopic pregnancies often present with abdominal pain and/or bleeding, and an adnexal mass.^{3 13–17} There were also asymptomatic cases detected only on ultrasound.^{18 19} A comprehensive history should be taken, including risk factors associated with heterotopic pregnancy, such as IVF with multiple ET, history of pelvic inflammatory disease, tubal surgery and endometriosis.⁸ Serum β -hCG has low utility due to the viable IUP in heterotopic pregnancies.²⁰ Accurate ultrasound diagnosis of non-tubal ectopic pregnancies is also challenging.¹² The Royal College of Obstetricians & Gynaecologists proposed an ultrasound criteria for abdominal ectopic pregnancies which includes: (1) absence of an IUGS, (2) absence of both an evidently dilated tube and a complex adnexal mass, (3) a gestational cavity surrounded by loops of bowel and separated by peritoneum and (4) a wide mobility similar to fluctuation of the sac particularly evident with pressure of the transvaginal probe towards the posterior cul-de-sac.^{21 22}

The index of suspicion for this patient must be elevated in view of the high β -hCG levels 2 weeks after ET. With such a high β -hCG level, double ET done and a single IUGS seen on scan, a conscious effort must be made to rule out a heterotopic pregnancy. Patients should be monitored for heterotopic pregnancies post-IVF ET with TVUS by trained sonographers as it has a high sensitivity for detection.^{2 23 24} The timing of the ultrasound scan is of great importance. This case was first seen at 6 weeks of gestation with only a single IUGS seen and subsequently presented 2 weeks later with heterotopic pregnancy diagnosed on ultrasound. Other cases reported also had initial ultrasound findings of a single IUGS at 5–7 weeks' gestation, and repeat ultrasound 1–2 weeks later revealed the ectopic pregnancy.^{3 18} At later gestation, the presence of an ectopic pregnancy may become more evident. Hence, it would be prudent to monitor patients with risk factors for heterotopic pregnancy by serial ultrasound scans.

If the diagnosis is still uncertain, and the patient is stable, other diagnostic imaging may be considered, such as MRI.²¹ MRI can be performed in stable patients to confirm the diagnosis and identify if the placenta has been implanted over

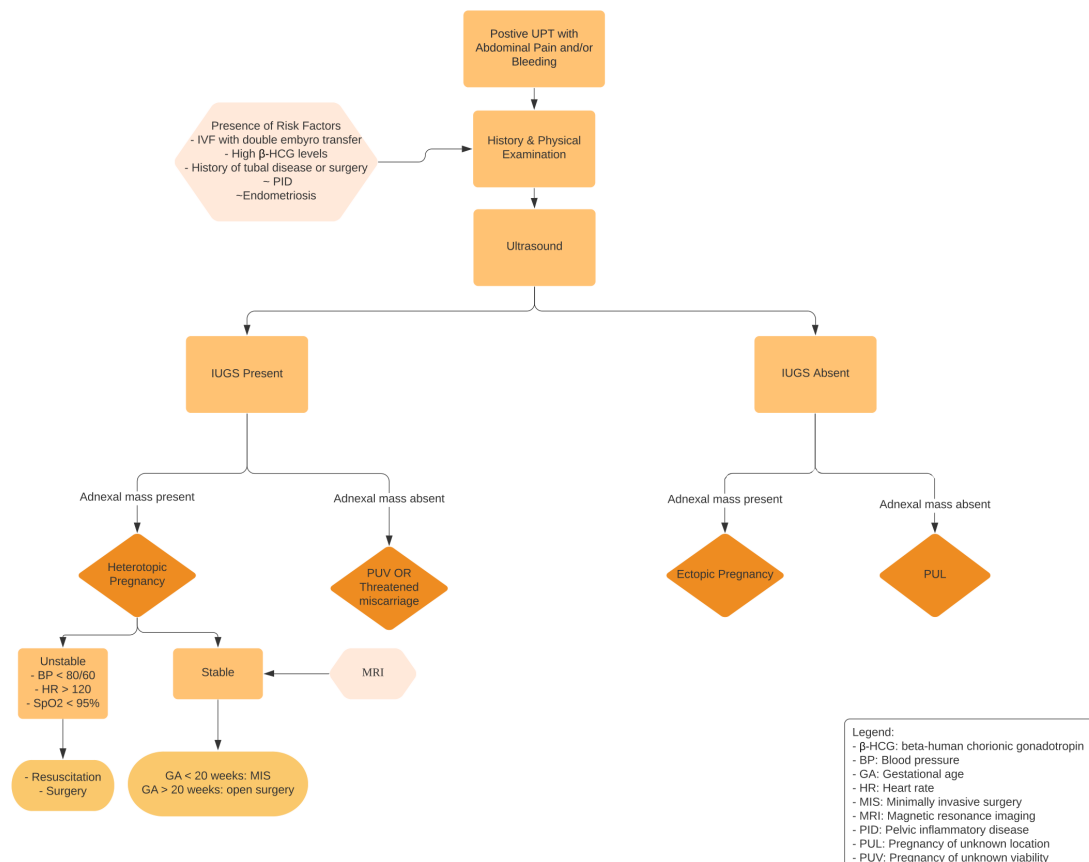


Figure 3 Approach to women with pain and bleeding in early pregnancy.

structures such as large vessels or bowel. It could also help to guide perioperative and operative considerations.²⁵ MRI of the pelvis has been used to precisely identify the location of the ectopic and to guide subsequent management.¹⁹

Management

Traditionally, management of the ectopic pregnancy would include conservative, medical or surgical methods. When managing heterotopic pregnancies, the IUP should be considered unless it is non-viable or undesired.²¹

Expectant management is rarely used except in certain stable patients, where the IUP is non-viable, or the ectopic is not implanted on essential structures such as major vessels.^{10 21} However, it is not routine management due to possible rupture of the ectopic as the abdominal pregnancy progresses. Five cases of heterotopic pregnancy managed conservatively have been reported. These cases were detected at an advanced gestational age and required hospitalisation for the remainder of the pregnancy with continuous monitoring and imaging at intervals. Hence, at advanced gestation, conservative management may be an option, with subsequent delivery of the IUP and abdominal ectopic at the same time.^{15 26–29}

Medical treatment with methotrexate should only be considered if the IUP is non-viable or undesired due to its teratogenic effects.^{30 31} However, it is also not routine management due to the high risk of treatment failure and potential adverse consequences of haemorrhage or rupture. Intracardiac potassium chloride or local hyperosmolar glucose injection with aspiration of the gestational sac is another possible intervention for stable patients. Four cases managed with intracardiac

potassium chloride injection were reported, of which three resulted in live births.¹⁹

Surgical resection of the ectopic pregnancy, via laparoscopy or laparotomy, remains the first-line treatment for both haemodynamically stable and unstable patients. Abdominal heterotopic pregnancy diagnosed at an early gestational age in stable patients should be managed laparoscopically. Laparotomy should be reserved for patients who are haemodynamically unstable and/or are at an advanced gestational age (more than 20 weeks' gestation).^{10 21 25} Seven cases diagnosed at 5–10 weeks' gestation were managed via laparotomy,^{14 16 17 32–34} and two diagnosed at 6–9 weeks' gestation were managed via laparoscopy.^{3 18}

Preoperatively, testing for haemoglobin and cross-matching for blood products are essential due to the propensity for blood loss during surgery.^{16 17 32} Fluid resuscitation and blood transfusions intraoperatively are usually required for resection of abdominal ectopic pregnancies.^{14 32} In this case, the ectopic was implanted on the USL. The principles of surgery remain largely similar to those involving the USL, such as deep infiltrating endometriosis surgeries. Identification of surrounding structures, such as the bowel, ureters, rectum, cervix and vagina, and major vessels would be essential for reduction of postoperative complications.^{35 36} In cases where there is a viable IUP, no intrauterine devices should be used for manipulation, and laparoscopic manipulation of the uterus should be avoided.²¹ Complete resection of POC should be ensured. Haemostasis can be secured via sutures, electrocoagulation or use of haemostatic agents. The use of tranexamic acid should be considered.³⁷ Adhesion barriers can be applied to reduce abdominal adhesions.³⁸

Postoperatively, given that surgery may increase the risk of miscarriage, an ultrasound scan to monitor the viability of the IUP should be performed.¹⁸ Progesterone (intramuscular and/or oral) could also be given to support the pregnancy.^{18 33}

Follow-up

Follow-up for resolution can be challenging as monitoring of serum β -hCG levels is unreliable with a viable IUP.³ Thus, patients should be followed up with serial ultrasound scans, with close follow-up initially due to the increased risk of miscarriage.¹⁸ Spontaneous miscarriage after surgery usually occurs in the following 2–4 weeks.^{14 39} In a retrospective study of 64 heterotopic pregnancies, 14.1% of patients had a miscarriage, and it occurred within 3 weeks of the treatment. The only significant risk factor for miscarriage reported was early gestation at time of treatment, while the method of treatment (laparoscopic surgery, ultrasound-guided potassium chloride injection or gestational sac aspiration and observation) was not a significant risk factor.⁴⁰ In other studies examining the outcomes of heterotopic pregnancies managed laparoscopically, two patients had missed miscarriage within 8–14 days of the procedure, while two had miscarriages after rupture of membranes at 15–16 weeks' gestation.⁴¹

The timing and mode of delivery, after treatment for abdominal ectopic pregnancy, should be guided by obstetric indications. Among the cases of abdominal heterotopic pregnancy, some patients were delivered by caesarean section at 36–38 weeks' gestation due to patient's choice or undisclosed indications.^{33 34} Normal vaginal delivery at 40 weeks' gestation has also been reported.¹⁹ In two retrospective reviews of a total of 29 women who underwent laparoscopic surgery for heterotopic pregnancies, 23 women had live births. Across the two studies, 12 women delivered via normal vaginal delivery, while 13 had caesarean sections. Indications for caesarean section included failure to progress, cephalopelvic disproportion and previous caesarean section.^{41 42}

Learning points

- ▶ Clinicians should have a high index of suspicion for heterotopic pregnancies particularly in patients who have multiple risk factors such as having undergone in-vitro fertilisation with double embryo transfer, high beta-human chorionic gonadotropin levels, history of tubal disease or surgery, including pelvic inflammatory disease and endometriosis. While the location of the ectopic is most commonly tubal, clinicians should also consider other locations such as abdominal sites of implantation.
- ▶ The timing of the ultrasound scan is important as heterotopic pregnancies may be missed if done too early. Hence, even when a prior ultrasound scan showed a single intrauterine gestation sac, heterotopic pregnancies cannot be ruled out in patients with relevant risk factors, presenting with abdominal pain and per vaginal bleeding.
- ▶ Surgical management is recommended, via either laparoscopy or laparotomy for resection of products of conception. Do anticipate blood loss with resection of the abdominal ectopic pregnancies, with adequate blood products made available intraoperatively.
- ▶ Patients should be followed up closely with repeat ultrasound done for viability of the intrauterine pregnancy, given the increased risk of miscarriage in the next 2–4 weeks after treatment.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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