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Heterotopic Pregnancy: A Case Report and Literature Review

Mahmoud Elzarka [1], Ritu Dalmia [1]

1. Obstetrics and Gynaecology, Royal Oldham Hospital, Oldham, GBR

Corresponding author: Mahmoud Elzarka, mahmoud.elzarka@nca.nhs.uk

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Abstract

Heterotopic pregnancy, the simultaneous presence of an intrauterine and an extrauterine gestation, is rare after spontaneous conception. We describe a 30-year-old woman, gravida 2, with a previous left tubal ectopic pregnancy treated with methotrexate, who presented at 5+3 weeks of gestation with vaginal spotting and mild lower abdominal pain. Transvaginal ultrasound showed a left adnexal mass measuring 22 x 16 x 18 mm and a fundal intrauterine sac-like structure (mean sac diameter of 10 mm) without a yolk sac or fetal pole, which was reported as a possible pseudosac. Serum human chorionic gonadotropin (hCG) was 10,292 IU/L. Laparoscopic left salpingectomy confirmed an unruptured tubal ectopic pregnancy, which was verified histologically. A positive urine pregnancy test at the routine three-week postoperative check led to an ultrasound scan showing a viable intrauterine pregnancy with a crown-rump length of 23 mm (9+0 weeks). This matched the gestational age of the intrauterine sac seen before surgery, confirming that the two pregnancies had coexisted. The pregnancy was later complicated by late-onset fetal growth restriction, preceded by abnormal uterine artery Doppler at 20 weeks, and a healthy female infant weighing 2,250 g (1.2nd centile) was delivered by planned caesarean section at 37+2 weeks. An intrauterine sac-like structure should be regarded as a possible early intrauterine pregnancy even when an ectopic pregnancy is clearly visualised, and the post-salpingectomy pregnancy test provides an important safety net.

Categories: Obstetrics/Gynecology, Radiology
Keywords: early pregnancy ultrasound, ectopic pregnancy, fetal growth restriction, heterotopic pregnancy, laparoscopic salpingectomy, pseudogestational sac, spontaneous conception, uterine artery doppler

Introduction

Heterotopic pregnancy refers to the coexistence of intrauterine and extrauterine gestations. After spontaneous conception, it is uncommon, with a frequently quoted incidence of approximately one in 30,000 pregnancies [1]. The incidence is considerably higher after assisted reproduction; a United States registry study identified 207 heterotopic pregnancies among more than 130,000 pregnancies conceived through assisted reproductive technology, approximately 1.5 per 1,000 [2,3]. Risk factors largely mirror those for ectopic pregnancy and include previous ectopic pregnancy, pelvic inflammatory disease, tubal surgery and smoking, although many spontaneous cases occur in women with no identifiable risk factor [4].

The diagnosis is frequently delayed. When an intrauterine pregnancy is identified, clinicians may be falsely reassured and the adnexa may not be examined closely; most published spontaneous cases have been diagnosed only after tubal rupture and haemoperitoneum [4,5]. The opposite pitfall, in which an obvious ectopic pregnancy leads to an early intrauterine gestational sac being interpreted as a pseudosac, is less often described. We report a spontaneous heterotopic pregnancy in which the intrauterine component was visible but uncharacterised at the time of surgery, and in which the diagnosis was established through routine postoperative follow-up. The report follows CARE guidelines [6].

Case Presentation

A 30-year-old woman, gravida 2 para 0, attended the early pregnancy assessment unit at 5+3 weeks of gestation by her last menstrual period with vaginal spotting and mild lower abdominal pain. Five months earlier, she had had a left tubal ectopic pregnancy at approximately five weeks of gestation, treated successfully with systemic methotrexate. She had previously used the combined oral contraceptive pill, which she stopped 10 months before this conception, and the pregnancy was conceived spontaneously without ovulation induction or assisted reproduction. She was a non-smoker with a body mass index of 30 kg/m^2. On examination, she was haemodynamically stable (heart rate 99 beats/min, blood pressure 134/80 mmHg, temperature 37.4 °C, respiratory rate 17/min, oxygen saturation 100%) and her abdomen was soft and non-tender.

Verbal informed consent for publication of this anonymised case report was obtained from the patient by telephone, as her care had been completed before the report was prepared, and this was documented in her medical records.

Transvaginal ultrasound, supplemented by a transabdominal scan that was limited by the overlying bowel, showed an anteverted uterus containing a sac-like structure at the fundus measuring 14 x 5 x 11 mm, with a mean sac diameter of 10 mm, equivalent to approximately five weeks of gestation (Figure *1A*). No yolk sac or fetal pole was seen, and the appearance was reported as either a very early intrauterine pregnancy or a pseudosac. In the left adnexa, superior to and separate from a normal left ovary, there was a heterogeneous, predominantly solid mass measuring 22 x 16 x 18 mm with a central cystic component and no prominent vascularity (Figures *1B*, *1C*). A small amount of free fluid was present in the pouch of Douglas. The right ovary was seen only transabdominally and appeared normal. A second opinion from a clinical specialist sonographer concurred that the appearances were suspicious of a left tubal ectopic pregnancy. Serum human chorionic gonadotropin (hCG) was 10,292 IU/L.

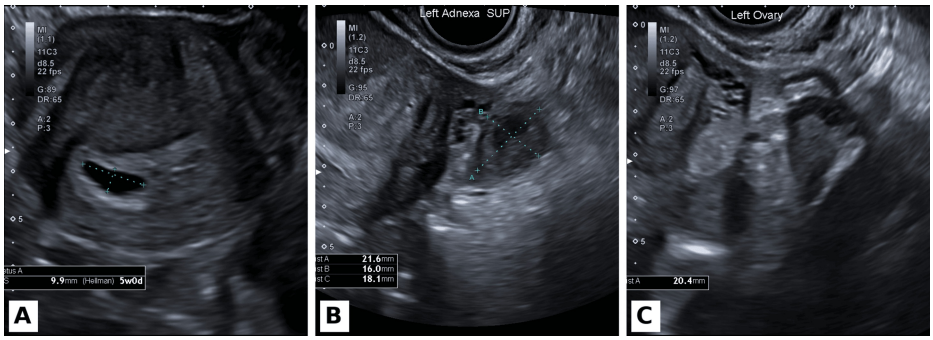


FIGURE 1: Transvaginal ultrasound at presentation (5+3 weeks by last menstrual period)

(A) Fundal intrauterine sac-like structure with a mean sac diameter of 9.9 mm and no yolk sac or fetal pole, reported as a possible early intrauterine pregnancy or pseudosac. (B) Heterogeneous left adnexal mass measuring 21.6 x 16.0 x 18.1 mm, with a central cystic component. (C) Normal left ovary (measuring 20.4 mm, labelled "Left Ovary"), located inferior to and separate from the adnexal mass shown in (B), confirming that the mass was extra-ovarian.

In view of the hCG level, which was above the threshold at which national guidance recommends surgery as first-line treatment, together with her recent ectopic pregnancy and the presence of free fluid, laparoscopic management was recommended [7,8]. Laparoscopic left salpingectomy was performed under general anaesthesia the following day using an open umbilical entry. A uterine manipulator was not used, and the uterus was not instrumented. At laparoscopy, the uterus was anteverted, mobile and slightly soft and globular. There was an unruptured left tubal ectopic pregnancy measuring approximately 2 cm, with about 50 mL of serosanguineous fluid in the pouch of Douglas. The right tube and both ovaries were normal, and there was no evidence of endometriosis. Blood loss was less than 50 mL. She was rhesus D positive and was discharged the same day with seven days of thromboprophylaxis and advice to perform a urine pregnancy test after three weeks, in accordance with national guidance [8]. The formal histopathology report described haemorrhagic material in the tubal lumen, decidualisation and chorionic villi, consistent with a tubal gestation.

Three weeks after surgery, the urine pregnancy test remained positive. She reported a small amount of brown vaginal discharge but no pain, and her abdomen was soft and non-tender. Transvaginal ultrasound showed a single viable intrauterine pregnancy with a crown-rump length of 23 mm, equivalent to 9+0 weeks, with fetal cardiac activity and normal adnexa (Figure *2*). Serum hCG was 89,108 IU/L. Back-calculation from the crown-rump length placed the gestation at 5+6 weeks at the initial scan, consistent with both her last menstrual period and the 10 mm intrauterine sac seen preoperatively. This excluded a new conception after surgery and confirmed that the intrauterine and tubal pregnancies had been present simultaneously.

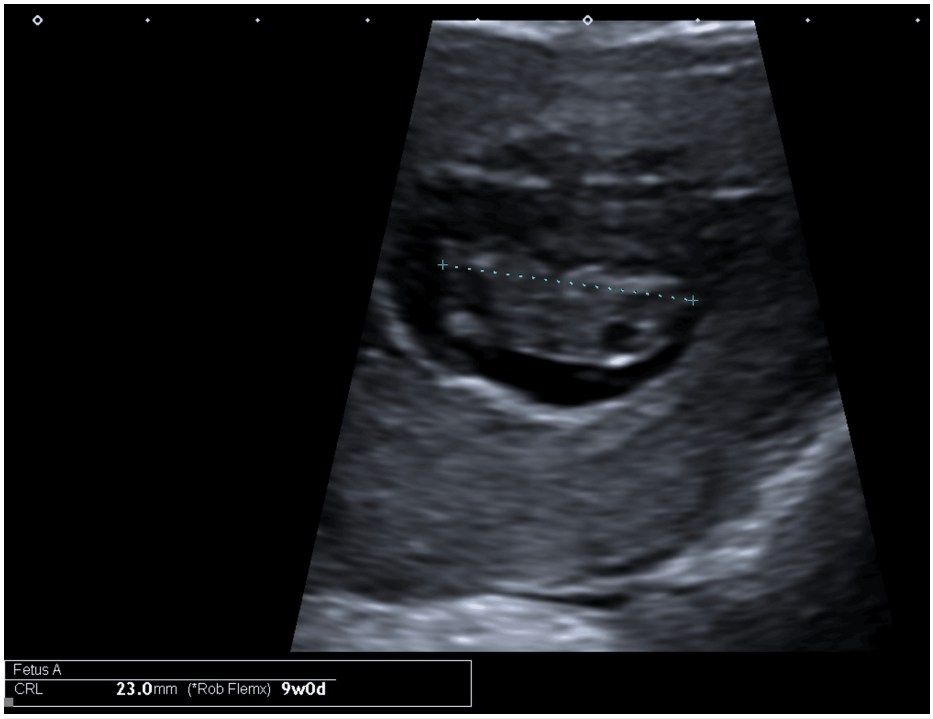


FIGURE 2: Transvaginal ultrasound three weeks after salpingectomy

Single viable intrauterine pregnancy with a crown-rump length of 23.0 mm, corresponding to 9+0 weeks of gestation.

The dating scan at 12 weeks was normal. A raised blood pressure at booking prompted a blood pressure series, which was normal, and she remained normotensive for the rest of the pregnancy. At 20+1 weeks, the anomaly scan showed normal fetal anatomy, an estimated fetal weight (EFW) of 321 g (34th centile), a posterior placenta clear of the os and normal liquor volume. Uterine artery Doppler screening was positive, with a mean pulsatility index above the 95th centile and notching of the left uterine artery waveform (Figure *3*), and serial growth scans were arranged from 28 weeks. She was not taking aspirin. An oral glucose tolerance test was normal.

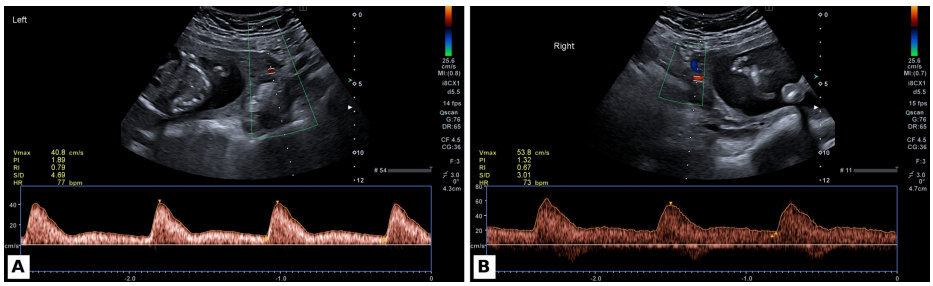


FIGURE 3: Uterine artery Doppler at 20+1 weeks

(A) Left uterine artery, pulsatility index 1.89, with an early diastolic notch. (B) Right uterine artery, pulsatility index 1.32. Mean pulsatility index 1.61

Serial ultrasound showed a progressive fall in fetal growth centile, from the 21st centile at 28+1 weeks to the 1.9th centile (EFW 2,003 g) at 35+1 weeks (Table *1*), with normal umbilical artery Doppler and liquor volume at every scan and normal fetal movements. Following multidisciplinary review at 36 weeks, when maternal haemoglobin was 99 g/L, birth was recommended at 37 weeks in line with national recommendations for an EFW below the third centile [9]. Induction of labour was offered; she declined and requested caesarean birth because of the small fetus. A planned lower segment caesarean section was performed at 37+2 weeks, with an estimated blood loss of 600 mL (preoperative haemoglobin 110 g/L). A healthy female infant was born weighing 2,250 g (1.2nd centile), with Apgar scores of 10 at one and five minutes. She was not admitted to the neonatal unit and received pre-feed blood glucose monitoring and newborn early warning observations according to the local low-birthweight protocol. Mother and baby had an uncomplicated postnatal course.

The placenta was not sent for histological examination. The clinical course is summarised in Table 2.

Gestation (weeks)	EFW (g)	Centile
20+1	321	34th
28+1	1,122	21st
31+1	1,465	6th
33+1	1,756	4th
35+1	2,003	1.9th
Birth, 37+2	2,250 (actual)	1.2nd

TABLE 1: Serial fetal growth

Umbilical artery Doppler and liquor volume were normal at every growth scan.

EFW: estimated fetal weight

Gestation	Findings	Action/outcome
5+3 weeks	Vaginal spotting, mild lower abdominal pain; stable observations. TVS: fundal intrauterine sac, MSD 10 mm, no yolk sac or fetal pole; left adnexal mass 22 x 16 x 18 mm; small free fluid. hCG 10,292 IU/L	Laparoscopic left salpingectomy the following day
10 days later	Histology: decidualised tubal tissue with chorionic villi	Tubal gestation confirmed
9+0 weeks	Positive urine pregnancy test. TVS: viable IUP, CRL 23 mm; normal adnexa. hCG 89,108 IU/L	Heterotopic pregnancy confirmed
12 weeks	Normal dating scan; raised booking BP	BP series normal
20+1 weeks	Normal anatomy; EFW 34th centile; uterine artery mean PI >95th centile with notching	Serial growth scans
28+1 to 35+1 weeks	EFW fell from 21st to 1.9th centile; normal umbilical artery Doppler and liquor	MDT: birth at 37 weeks
37+2 weeks	IOL declined; planned caesarean section; EBL 600 mL	Female, 2,250 g (1.2nd centile), Apgar 10 and 10; no neonatal unit admission

TABLE 2: Timeline of clinical events

BP: blood pressure; CRL: crown-rump length; EBL: estimated blood loss; EFW: estimated fetal weight; hCG: human chorionic gonadotropin; IOL: induction of labour; IUP: intrauterine pregnancy; MDT: multidisciplinary team; MSD: mean sac diameter; PI: pulsatility index; TVS: transvaginal ultrasound

Discussion

Heterotopic pregnancy after spontaneous conception remains rare. The traditional estimate of 1 in 30,000 pregnancies predates widespread use of assisted reproduction and transvaginal ultrasound [1], and the incidence is substantially higher after ovulation induction and in vitro fertilisation [2,3]. In a systematic review of 18 reports of spontaneous heterotopic pregnancy with a live intrauterine gestation, Oancea et al. found that most women had no identifiable risk factor, that diagnosis was made at a median of eight weeks, and that tubal rupture had usually occurred by the time of diagnosis [4]. Our patient differed in two respects: she had a significant risk factor, a previous ectopic pregnancy on the same side managed medically with tubal conservation, and her ectopic pregnancy was identified early, before rupture.

The principal learning point concerns the interpretation of the intrauterine sac-like structure. The teaching

that a pseudosac is a common finding in ectopic pregnancy originates largely from the era of transabdominal imaging. With modern transvaginal ultrasound, a round or oval intrauterine fluid collection in a woman with a positive pregnancy test is far more likely to represent an early gestational sac than a pseudosac [10]. The absence of a yolk sac or embryo at a mean sac diameter of 10 mm does not in itself indicate an abnormal pregnancy [11], and the intradecidual and double decidual signs show only moderate interobserver reliability, so their absence does not exclude an intrauterine pregnancy [12]. In this case, the preoperative sac size, the last menstrual period and the later crown-rump length all corresponded to the same gestational age, indicating that the reported possible pseudosac was the intrauterine pregnancy. The identification of an extrauterine pregnancy should therefore not lead to an intrauterine sac being dismissed, particularly in women at increased risk of ectopic pregnancy [4,5]. Recognising the possibility of heterotopic pregnancy before surgery allows the woman to be counselled that an intrauterine pregnancy may continue, avoids uterine instrumentation, and should prompt a planned early follow-up scan.

Recognition also determines treatment. Systemic methotrexate is contraindicated when a coexisting intrauterine pregnancy is present or cannot be excluded [7,8]. Our patient had recently been treated successfully with methotrexate and might reasonably have favoured the same approach; however, her hCG level of over 10,000 IU/L made surgery the recommended first-line option, which avoided exposing the intrauterine pregnancy to a teratogenic and potentially abortifacient drug [8]. Laparoscopic salpingectomy is the preferred treatment for the tubal component of a heterotopic pregnancy, whereas local injection of potassium chloride or hyperosmolar glucose is generally reserved for non-tubal sites such as interstitial, cervical or caesarean scar implantation [7]. Minimal handling of the uterus is advised [4], and in this case, no uterine manipulator was used. Intrauterine pregnancies have continued to term after both laparoscopic and open surgery for spontaneous heterotopic pregnancy [4,13-16], including term vaginal birth after laparoscopic salpingectomy [15].

Serum hCG is of limited value in heterotopic pregnancy because the trophoblast of both gestations contributes to the circulating level. Here, the diagnosis was made through the post-salpingectomy urine pregnancy test recommended by the National Institute for Health and Care Excellence [8]. This simple step, intended to detect persistent trophoblast, also identified the ongoing intrauterine pregnancy. Without it, the diagnosis might have been delayed further, for example, if the brown discharge had been attributed to postoperative bleeding.

Once the ectopic component has been treated, outcomes for the intrauterine pregnancy are generally favourable. Approximately two-thirds continue to live birth and about one-third miscarry [3,4]. In a large registry cohort, heterotopic pregnancies had higher rates of spontaneous and induced abortion than intrauterine-only pregnancies, but among pregnancies that reached live birth, perinatal outcomes, including preterm birth and low birthweight, did not differ [2]. It is therefore unlikely that the heterotopic pregnancy or its surgical treatment directly caused the growth restriction in our patient. The fall in EFW from the 34th centile at 20 weeks to below the third centile after 32 weeks meets the consensus definition of late-onset fetal growth restriction [17], and the raised uterine artery pulsatility index with notching at 20 weeks, a recognised marker of impaired placentation and of increased risk of small-for-gestational-age birth [18], offers a more plausible explanation. Planned birth between 37+0 and 37+6 weeks for an EFW below the third centile without additional concerning features is consistent with the Saving Babies' Lives care bundle [9], and the birthweight of 2,250 g (1.2nd centile) confirmed the accuracy of the antenatal estimate.

The strengths of this report include histological confirmation of the tubal gestation and consistent dating, by last menstrual period, preoperative sac size and crown-rump length, which establishes that the two pregnancies coexisted. Its limitations are those of a single retrospective case: the position of the sac relative to the endometrial midline was not documented at the time, no planned early follow-up scan was arranged after surgery, and the placenta was not examined histologically, so a placental cause for the growth restriction could not be confirmed.

Conclusions

Spontaneous heterotopic pregnancy is rare but should be considered whenever an intrauterine sac-like structure coexists with an adnexal mass, particularly in women with a previous ectopic pregnancy. An intrauterine fluid collection in a woman with a positive pregnancy test should be regarded as a possible early intrauterine pregnancy until proven otherwise. This influences counselling, excludes methotrexate, guides surgical technique and should prompt early follow-up.

In this case, adherence to the routine post-salpingectomy pregnancy test identified the ongoing pregnancy. After timely laparoscopic treatment of the ectopic component, the intrauterine pregnancy can be expected to continue, with subsequent antenatal care guided by standard obstetric indications rather than by the heterotopic pregnancy itself.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Mahmoud Elzarka

Drafting of the manuscript: Mahmoud Elzarka

Concept and design: Ritu Dalmia

Critical review of the manuscript for important intellectual content: Ritu Dalmia

Supervision: Ritu Dalmia

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Not applicable issued approval N/A. Formal ethical approval was not required for this single anonymised case report. Verbal informed consent for publication was obtained from the patient and documented in her medical records. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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