

CASE REPORT

Persistent increase of β -hCG level after salpingectomy in tubal pregnancy: Good or bad news?

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Abstract

Heterotopic pregnancy is a rare event in natural conception (1:30000). We describe a case of a 36-year-old nulliparous. She presented to our department in the 4+6 gestational week with two simultaneous pregnancies intrauterine and extrauterine. Here, we compare treatment options and ultrasound findings to help examiners avoid inadequate therapeutic approaches.

KEYWORDS

chorionic gonadotropin, pregnancy, ectopic pregnancy

1 | INTRODUCTION

Heterotopic pregnancy is a rare event in natural conception (1:30 000). We describe a case of a 36-year-old nulliparous woman. She presented to our department in the 4 + 6 gestational week with two simultaneous pregnancies, intrauterine and extrauterine. Here, we compare treatment options and ultrasound findings to help examiners avoid inadequate therapeutic approaches.

Ectopic pregnancy (EP) describes an extrauterine pregnancy (EUP) without a viable intrauterine pregnancy (IUP) and the ectopic IUP (eg, cervical pregnancy or *cesarean* scar pregnancy). It is the leading cause of maternal death during the first trimester of pregnancy. In contrast, a heterotopic pregnancy (HP) is the occurrence of two simultaneous pregnancies—most common IUP and EUP. While relatively seldom with assisted reproductive techniques (1%-3%),¹ it is exceptional in natural conception with a frequency of about 1:30 000 pregnancies.²

Risk factors for HPs are prior EP, history of pelvic inflammatory disease or gynecologic surgery, congenital uterine anomalies, use of an intrauterine device, in vitro fertilization, and endometriosis or nicotine abuse. HP is in approximately 70% of the cases detected during gestational weeks 5-8, whereas 20% of the cases were detected during weeks 9-10 and only 10% after gestational week 11.¹ Symptoms can

be acute or nonacute with pelvic pain and vaginal spotting; however, up to 50% of the patients are asymptomatic.¹ The evaluation of patients suspected to have an EP includes a quantitative measurement of serum β human chorionic gonadotropin (β -hCG) with or without evaluation of progesterone levels and a transvaginal sonography.³

2 | CASE

A 36-year-old nulliparous woman with a previous history of a complete tubal abortion presented to our emergency ward during her second pregnancy describing lower abdominal pain without fever or spotting for four hours in the 4 + 6 weeks of pregnancy. No relevant underlying medical conditions were known, and upon admission, the quantitative measurement of serum β -hCG revealed 10824 IU/L.

The transvaginal ultrasound showed a moderate amount of free fluid in the pouch of *Douglas* and an intrauterine sac without yolk sac or an embryonal structure, slightly elongated and central within the endometrium (Figure 1A). Furthermore, we saw a highly suspicious structure for an EUP along the right fallopian tube: a complex extraovarian cyst with a ring of fire sign (Figure 2A).

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Due to the clinical history of the pregnant patient with acute lower abdominal pain, moderate free intraperitoneal fluid, a high suspicion of an EUP in the right fallopian tube, and the status after tubal abortion on the right side, she underwent diagnostic laparoscopy. Herewith, an EUP in the right fallopian tube was clearly detected (Figure 2B). Considering that the laparoscopic tube-preserving procedure (milking-out) was unsuccessful together with the patient's prior medical history, a salpingectomy on the right side was performed. Postoperative pathological examination of the fallopian tube

confirmed an EP with a hematosalpinx without evidence of wall perforation, molar pregnancy, inflammation, dysplasia, or malignancy.

The patient recovered well from the intervention, but on the third postoperative day, the control of β -hCG level showed an increase to 18859 IU/L. In a transvaginal ultrasound, the intrauterine sac remained in the same position but now with a putative embryonic structure—so far without a heartbeat. On the fourth postoperative day, the ultrasound showed a positive heart action for the first time and a crown-rump length (CRL) of 0.26cm. The patient was discharged on that day with the rare diagnosis of a HP without any symptoms. A follow-up on the ninth postoperative day in the mathematical 6 + 1 week of pregnancy confirmed the intact IUP with a CRL of 0.74cm and a visible heartbeat (Figure 1B).

After a complication-free pregnancy, in the 38 + 0 week the patient gave birth to a timely developed male (3470g, 51cm) spontaneously and without problems.

3 | DISCUSSION

A HP occurs when two pregnancies develop simultaneously usually as result of multiple ovulation events.⁴ It can be a potentially fatal condition because of the risk of rupture and bleeding from the EP, which is in 95% located in the fallopian tubes and in 5% situated elsewhere outside the uterine cavity.¹ On the other hand, as some treatment options for managing an isolated EUP can be toxic to a healthy pregnancy, the intact IUP may be at risk if it is misclassified as a pseudogestational sac, which was the misapprehension given at first in this case.

As it is in many other rare medical conditions, adequate diagnostic tools and knowledge are key to proper diagnosis. Herein, serum quantitative β -hCG level and the transvaginal/ transabdominal ultrasound are the most important methods. Although the detection of an EUP *via* ultrasound is sometimes tough, it was initially successful in this case. But medical practitioners should have focused in more detail on examining the intrauterine sac. Only one in ten EUPs present a pseudogestational sac.⁵ It is a well-described sonographic

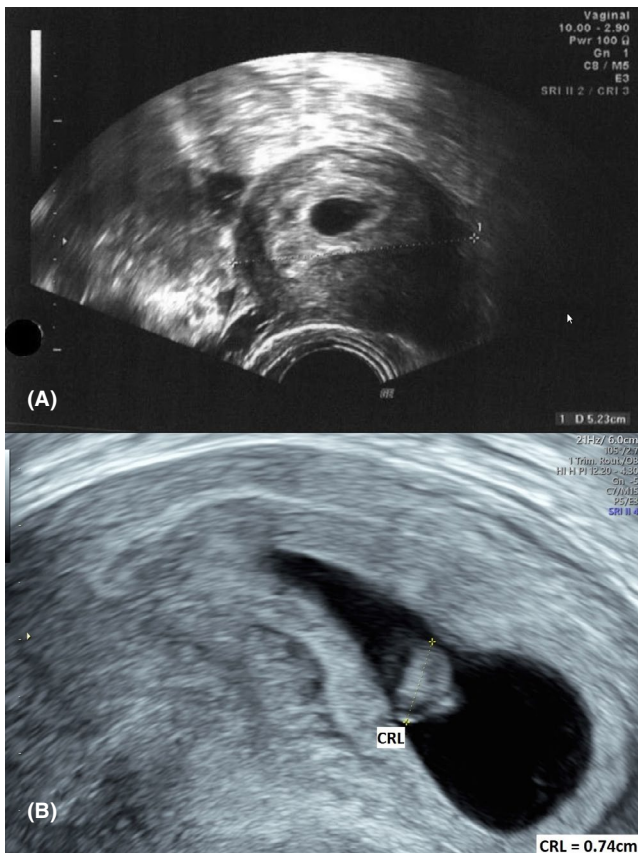


FIGURE 1 A, Transvaginal ultrasound in 4 + 6 gestational weeks directly prior to surgery aiming to differentiate between gestational and pseudogestational sac within the uterus. At this time point, no yolk sac or fetal pole was seen. B, Nine days later in 6 + 1 gestational week, an embryo with positive heart action and a CRL of 0.74cm was visible

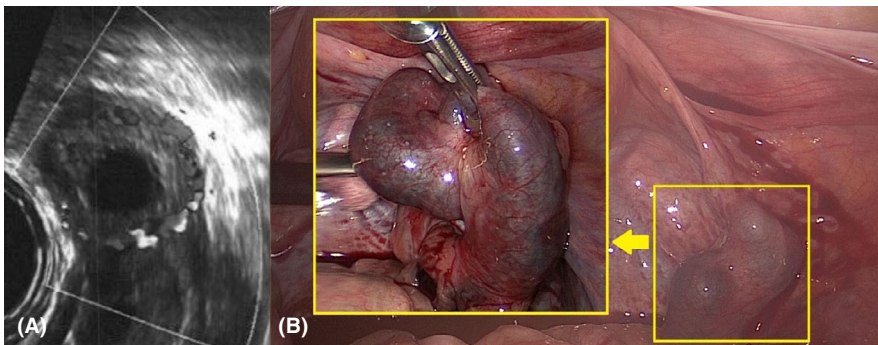


FIGURE 2 A, In 4 + 6 gestational weeks, the transvaginal ultrasound showed a highly suspicious structure for an EUP along the right fallopian tube: a complex extraovarian cyst with a ring of fire sign. B, Laparoscopic situs confirmed unruptured EP in the ampullary portion of the right fallopian tube

sign, which represents a decidual reaction surrounding intrauterine fluid/ hemorrhage without a yolk sac or fetal pole, no double decidual sac, a central position within the endometrium, and an elongated shape. *Puttagunta and Lee (2019)* compared the main sonographic findings in a genuine gestational sac and a pseudogestational sac (Table 1).⁵ The intrauterine sac of our patient presented without yolk sac and/or an embryonic structure only slightly elongated and is roughly central within the endometrium. A double decidual sac was not clearly detectable. Taken together, we interpreted it as a pseudogestational sac (Figure 1A). These findings together with the free fluid in the pouch of *Douglas* and the highly suspicious structure on the right fallopian tube with some of the most typical characteristics of an EP (a complex extraovarian cyst and a ring of fire sign; Figure 2A), led us to a diagnostic misconception of an EP alone.

But even with the presence of a simultaneous IUP, the diagnostic laparoscopy was indicated in this case due to the referred pain and intraabdominal fluid. Herewith, we were able to confirm and treat the EUP, without damaging the IUP. Currently, surgical mortality is not significantly higher in pregnant women than in those who are not; however, the awareness of the physiological changes during pregnancy and the resulting pharmacological adaptations are essential for the surgeon and the anesthesiologist.⁶ This should be kept in mind whenever a HP cannot be completely excluded. Anesthesia should avoid pharmacological contraindications during gestation, as well as damaging any reproductive organs. For example, the *corpus luteum graviditatis* must be protected. In parallel, *Gao et al 2019* described the surgical treatment as occasionally challenging for three reasons: difficulties in controlling the intraoperative blood loss, a possible proximity of an interstitial EP to the healthy IUP, and maintenance of uterine structural integrity to support the ongoing IUP.⁷

In the absence of acute symptoms, there are at least two other options for the management of HP besides surgical

treatment with salpingectomy or salpingostomy. Some cases can resolve spontaneously in hope of tubal abortion, without any intervention.⁸ However, strict follow-up is necessary together with the control of symptoms, sonographic findings, and β -hCG value. In some situations, for example, in areas with poor medical supply, hospitalization might be necessary to track these aspects, while sometimes an outpatient concept is acceptable. The second option involves the injection of drugs locally into the EP *via* laparoscopy or transvaginal sonography. This is a good choice for hemodynamically stable patients with minimal symptoms and the absence of free fluid within the peritoneal cavity. The transvaginal ascent is favorable but highly demanding for intrauterine EPs, such as a cervical or cornual pregnancy, in contrast to an intact IUP. Common EUPs as part of a HP can be treated *via* the laparoscopic ascent. Potassium chloride and hyperosmolar glucose are two alternative options. According to *Raughley and Frishman (2007)*, potassium chloride provides a clear end point with cessation of cardiac activity if existing and hyperosmolar glucose is a large molecule that creates an osmotic effect, leading to dehydration of the trophoblastic tissue.⁹ They are safe agents with no risk of systemic toxicity to the remaining gestation. Methotrexate, mifepristone, and prostaglandins cannot be used as a result of their putative harmful effects on the viable IUP.^{10,11}

Considering all treatment possibilities, we recommend to correlate development of serum β -hCG level with clinical findings: reaching zero if the putative IUP did not develop adequately and resulting in abortion or increasing in a remaining intact IUP.¹² Luckily, if diagnosed early, HP has a favorable prognosis. Data show that more than half of these cases proceed as a normal IUP after treatment of the EUP.¹³

The lesson to learn from this case report is that once a EUP is detected, clinicians tend to forget the possibility of a coexisting IUP or classify this as a pseudogestational sac. Examiners should take extra care when performing the ultrasound in all women of reproductive age with clinical symptoms, since the presence of an EUP does not exclude an IUP and *vice versa*, even if it is an extremely rare situation.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Pedro Cristiano Pinto Ribeiro: contributed to conception and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision

TABLE 1 Differences in sonographic findings between intrauterine gestational sac in IUP and pseudogestational sac in EUP compared with the first ultrasound in our case in 4 + 6 gestational weeks: + = accordance, - = no accordance, and \pm = partial or unclear accordance (modified according to *Puttagunta and Lee 2019*⁵)

	Gestational sac	Pseudogestational sac
Yolk sac or fetal pole	Yes (-)	No (+)
Double decidual sac	Yes (\pm)	No (\pm)
Location within the endometrium	Eccentric (\pm)	Central (+)
Shape	Rounded (-)	Elongated (\pm)
Arterial flow on color Doppler	Yes (-)	No (+)

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ETHICS STATEMENT

This case report is published with the patient's permission.

DATA AVAILABILITY STATEMENT

The data and materials generated and analyzed during the current analysis are available from the corresponding author on reasonable request.

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