

# Heterotopic pregnancy diagnosed before the onset of severe symptoms: case report

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## Summary

**Background:** A heterotopic pregnancy (HP) is an extremely rare disease that represents the simultaneous occurrence of two or more implantation sites in the uterus and extrauterus. Early diagnosis of HP is difficult because of the presence of an intrauterine pregnancy (IUP). In most cases, a precise diagnosis was made after symptoms develop through the rupture or bleeding of the ectopic pregnancy (EP). The authors present a case that was successfully diagnosed as an undemonstrative HP. **Case:** A 24-year-old multiparous woman became pregnant after taking clomiphene citrate. At ten weeks of pregnancy, an ultrasonography revealed gestational sacs containing fetuses in the uterus and the right adnexal region, respectively. The patient was diagnosed as having a HP and an emergency right tubal resectomy was performed. The IUP progressed normally and the fetus was delivered at 37 weeks of pregnancy. **Discussion:** Even if a gestational sac can be confirmed in the uterus, a careful ultrasonographic examination should always be considered to determine the presence of a concurrent extrauterine pregnancy.

**Key words:** Heterotopic pregnancy; Ectopic pregnancy; Ultrasonography.

## Introduction

Heterotopic pregnancy (HP) is an uncommon clinical entity and a diagnosis of HP remains challenging. A rupture of ectopic pregnancy (EP) causes catastrophic consequence due to massive bleeding. In the majority of cases, the diagnoses can be made only after the onset of lower abdominal pain and/or hypovolemic shock that develops suddenly. The authors report a case of asymptomatic HP which was successfully diagnosed.

## Materials and Methods

A 24-year-old woman, 3 gravida, 1 para, 2 spontaneous abortion, became pregnant. The reminder of the past history and family history were not contributory. The patient had undergone the induction of ovulation with clomiphene citrate for her ovulatory disturbance. At her antecedent clinic, a normal pregnancy had been diagnosed.

At ten weeks and two days after her last menstrual period, a transvaginal ultrasonography (TVUS) revealed a viable intrauterine pregnancy (IUP) and the presence of right tubal EP simultaneously. The patient was transferred to this hospital for further examination of HP.

On admission, blood pressure was 104/70 mmHg, and heart rate was 72 beats/min. Body temperature was 37.4°C. The patient did not complain of any lower abdominal pain or abnormal genital bleeding. Laboratory profile showed that red cell counts were  $453 \times 10^4/\mu\text{l}$ , hemoglobin 12.3  $\mu\text{g/dl}$ , and hematocrit 37.3%. Chlamydia IgA antibody was negative, whereas the IgG antibody was positive.

Pelvic examination showed that the uterus was enlarged up to the size of a goose egg. The patient complained of no tenderness in the uterus and bilateral adnexal regions. TVUS revealed a 35 mm-sized, viable fetus corresponding to ten weeks in the normal uterine cavity, as well as one more 30 mm-sized fetus without fetal heart movement in the right adnexal region (Figure 1). There

was no ascites in the cul-de-sac. Magnetic resonance imaging (MRI) of the pelvis clearly displayed a gestational sac with a high intensity in the intrauterine cavity and a cystic sac-like structure in the right adnexal region on T2-weighted image (Figure 2).

On the basis of these imaging technologies, she was diagnosed as having a HP. The patient was informed of the possibility of a life-threatening complication accompanied by the rupture of EP. She underwent an emergency laparotomy under spinal anesthesia. Laparotomy revealed the bulging at the right ampulla of the fallopian tube, confirming a right tubal pregnancy. Resectomy of the right tube was performed (Figure 3). No severe adhesion was detected in the abdomen, and intraoperative blood loss was minimal. Postoperatively, 50 mg progesterone was injected intramuscularly everyday as a luteal support in order to maintain the intrauterine normal pregnancy. Her postoperative course was uneventful with no sign of threatened abortion and was discharged from the hospital eight days postoperatively.



Figure 1. — Simultaneous extrauterine tubal pregnancy (arrow-head) and intrauterine normal pregnancy (arrow) seen on abdominal ultrasonography at ten weeks of pregnancy.

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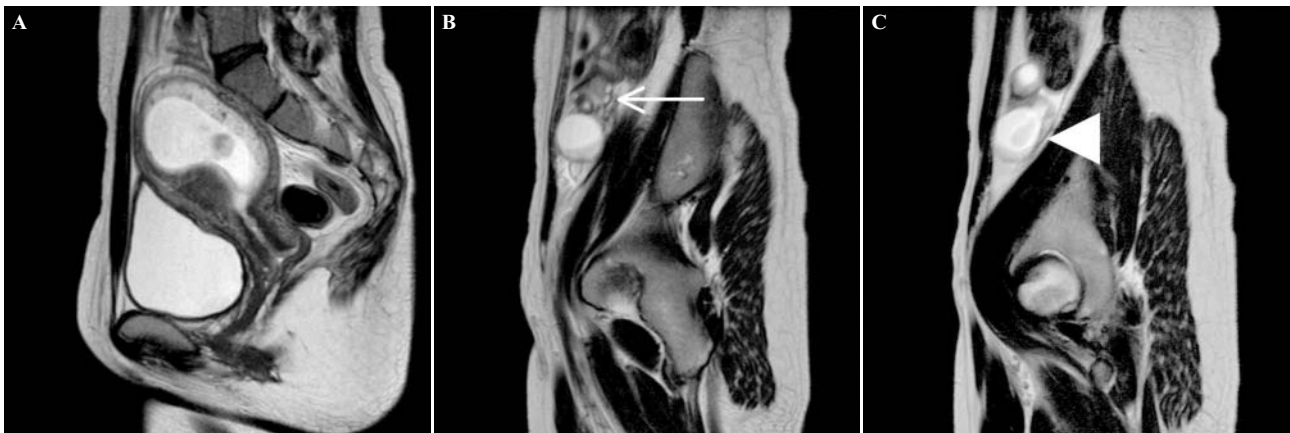


Figure 2. — T2-weighted images of MRI of the pelvis show (a) gestational sac of high-signal intensity in the intrauterine cavity, (b) the right ovary (arrow), and (c) a cystic lesion of high-signal intensity located between the uterus and the right ovary, indicating tubal pregnancy (arrowhead).

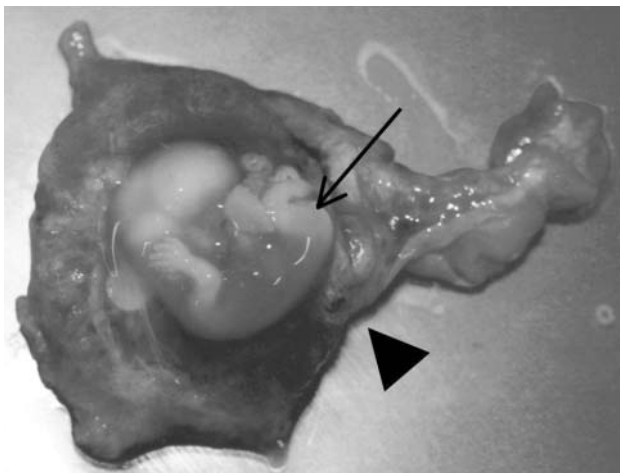


Figure 3. — Gross findings of the right ampulla pregnancy (arrowhead) and the fetus (arrow).

Thereafter, she was transferred back to her antecedent clinic. She was admitted again for five weeks from 29 to 34 weeks of gestation in this clinic under the risk of a preterm delivery and received continuous intravenous administration of ritodrine hydrochloride. At the 37<sup>th</sup> week and four days of pregnancy, she went into labor spontaneously and delivered a female baby with a birth weight of 2,748 g. An Apgar score was 8 at one minute and 9 at five minutes. The patient and her baby had uneventful postpartum courses.

## Discussion

HP is an extremely rare event with its occurrence being one per 30,000 pregnancies [1]. Both assisted reproductive technologies including in vitro fertilization and embryo transfer (IVF-ET) which insert several fertilized ova into the uterine cavity, and the induction of ovulation are reported to increase the incidence of HP up to one percent [2].

The risk factors causing HP are similar with those causing single EP and are as follows: tubal factors such as uni-

lateral tubal occlusion, a past history of ectopic pregnancy, hydrosalpinx, and the pelvic inflammatory factor such as previous intrapelvic operation including myomectomy, intrauterine device (IUD), and a past history of therapy for infertility [3]. In this case, the patient showed a positive chlamydia IgG antibody, suggesting that the past history of pelvic inflammatory disease could be one of the reasons to cause HP, whereas the use of ovulation-inducing agents seemed also to be the reason to cause this disease.

It remains a clinical challenge to diagnose unexpressed HP at an asymptomatic status. Tal *et al.* reported that almost 70% of HP were detected between five and eight weeks of pregnancy and that 20% were detected between nine and ten weeks of pregnancy [2]. The remaining ten percent were detected after 11 weeks of pregnancy [2].

The main symptoms of the HP include abdominal pain, signs of peritoneal irritation, adnexal tumors, and uterine swelling. Among them, the most frequent symptom to detect and diagnose this disease is abdominal pain, which occurs in 72% of patients, followed by 51% of abnormal genital bleeding, 44% of bleeding in the peritoneal cavity, and development of hypovolemic shock after the rupture of HP [4]. In most cases, HP can be diagnosed only after the patients become symptomatic, while this patient was fortunately diagnosed at an asymptomatic status.

The EP portion in the case of HP is different from that of the single EP, which often lacks abnormal genital bleeding. It is suggested that because an intrauterine normal pregnancy occupies the intrauterine cavity, bleeding accompanied by the rupture of tubal pregnancy does not flow into the vagina, but into the intra-abdominal space via the fallopian tubes or through the point of bleeding. Furthermore, the EP generates genital bleeding due to unstable secretion of human chorionic gonadotropin (hCG). In contrast, this bleeding happens less frequently in HP, since the normal IUP can maintain the secretion of hCG [5].

TVUS is useful to diagnose this disease. The definite diagnosis of HP can be made by the simultaneous detection of EP and normal IUP. However, such cases are very rare. Unlike single EP, the presence of normal IUP may make it

more difficult to detect another EP portion in the HP. The authors employed MRI as a complementary tool for the diagnosis of the HP in addition to TVUS. MRI was found to be useful for the evaluation of the location of an extrauterine gestational sac (GS), as was TVUS.

Van Dam *et al.* reported that successful rates to diagnose HP correctly with the detections of GS or embryo preoperatively was 14% and that 62% of the cases did not show any abnormal findings [5]. Barrenetxea *et al.* demonstrated that almost 74% of HPs were diagnosed after laparoscopic surgery or open laparotomy, while only 26% could be diagnosed correctly preoperatively [3]. On the other hand, ovarian swelling due to ovarian hyperstimulation syndrome (OHSS) may make it difficult to detect the EP portion around the fallopian tubes, and OHSS also makes it difficult to distinguish between pooling ascites and bleeding in the peritoneal cavity, which leads to a misdiagnosis of this disease. However, even in such a case, culdocentesis may be useful to distinguish between ascites and bleeding in the pelvis, and MRI can distinguish between tubal pregnancy and ovarian swelling in the case of OHSS. Tamai *et al.* reported that MRI provided a better delineation when ultrasonographic findings in EP were indeterminate and that the key MRI features of EP typically appeared as a cystic sac-like structure, frequently associated with surrounding acute hematoma showing a distinct low intensity on T2-weighted image [6].

Surgery is the mainstay for HP. Especially in the case of tubal pregnancy, tubal resectomy is the most common therapy for this disease. On the other hand, in the case of single EP, injection of methotrexate (MTX) into the muscle could be one of the choices for effective therapy. However, in the case of the HP, the MTX injection could not be the choice, considering that MTX has a toxic effect on the intrauterine fetus. Transvaginal local injections of potassium chloride (KCl) or hyperosmolar glucose have been reported for the less invasive and conservative treatment of HP. These therapies are adapted for patients who demonstrate severe abdominal symptoms or instability of vital signs, but do not show intra-abdominal bleeding. However, regarding KCl injection, its safety with respect to the fetus in uterus has not yet been proved. Goldstein *et al.* reviewed and analyzed eleven cases who underwent transvaginal KCl injection therapy, and reported that six in eleven cases (55%) followed hydrosalpinx or acute abdomen, and salpingectomies were finally performed [7]. On the other hand, Jefferey reported two cases that had achieved a successful result after transvaginal local injection of high-dose glucose [8]. More accumulation of cases is expected to warrant the safety of KCL therapy.

The reports regarding the prognosis of the intrauterine fetus are rare. Rizk *et al.* reported that only one case among the ten cases of the HP caused abortion after therapy [9], while Rojansky *et al.* reported that 70% of the patients could

succeed with living babies [4]. According to the report of Clayton *et al.*, IUP in the case of the HP had about 2.1 times higher risk of abortion compared with normal single pregnancy, however they could not find any significant difference in the following pregnancy risk between the HP patients who passed the risk of abortion and normal pregnancy [10].

In conclusion, early diagnosis and early therapy for HP may offer a better prognosis for HP patients who overcome the abortion risk at the early stage of pregnancy. The authors experienced the patient who was successfully diagnosed as having an undemonstrative HP. Although rare, an awareness of HP is important to prevent a delayed diagnosis and determine a prompt and adequate treatment option at the asymptomatic stage, particularly when the patient has conceived with artificial reproductive technologies. A careful ultrasonographic survey for the presence of concurrent EP is important, even if normal pregnancy is confirmed in the uterus.

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