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*Case Report*

# Progressive intrauterine twin pregnancy after surgical treatment of cornual heterotopic pregnancy: a report of two cases and literature review

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**Abstract:** One case was managed by resection of the cornual pregnancy by laparotomy; the other was treated with ultrasonographically guided transvaginal injection of KCl into the ectopic gestation. Complete ablation of the cornual pregnancy. Both women had no complications during their pregnancies. Cesarean section was performed in different indications and allowed the birth of two living infants. Both surgical and conservative treatment of an ectopic pregnancy can be adopted in accordance with patient's condition. The both treatment permitted the development of the intrauterine pregnancy. The risk of heterotopic pregnancy is directly related to the number of embryos transferred.

**Keywords:** Heterotopic pregnancy, IVF-ET, surgical treatment, ultrasonographic guidance-KCl injection, intrauterine pregnancy outcome

## Introduction

Heterotopic pregnancy is defined as the coexistence of an intrauterine pregnancy and an ectopic pregnancy [1]. The reported incidence of heterotopic pregnancy in a spontaneous cycle is approximately 1:7000 to 1:30000 women in the general population. However, the incidence of heterotopic pregnancy has increased to 1-2.9% since the development of assisted reproductive technologies (ART) procedures such as in vitro fertilization (IVF) and embryo transfer (ET) [2]. Few cases of triplet pregnancy with a combination of twin intrauterine pregnancy and a cornual pregnancy have been described [3]. However, this coexistence increases the complexity of the diagnosis and management for preserving the lives of both the mother and of the intrauterine pregnancy.

Here, we present two cases of a heterotopic triplet pregnancy with the development of a twin intrauterine pregnancy and unilateral cornual pregnancy. Both surgical and conservative treatment allowed us to permit the development of the intrauterine pregnancy and the birth of two sets of twins.

## Materials and methods

This study was approved by The Ethics Committee of Women's Hospital, School of Medicine, Zhejiang University. Participants have provided their written informed consent to participate in this study.

## Case reports

### *Case 1*

The patient was a 31-year-old woman, gravida 1, para 0, who had been treated for secondary infertility for the past 2 years due to mixed causes (tubal factor combined with asthenospermia). The patient had an spontaneous ectopic pregnancy which a right salpingectomy was performed three years ago.

One cycle of long course of ovarian stimulation was initiated. A total of 15 oocytes were retrieved, of which 13 were successfully fertilized

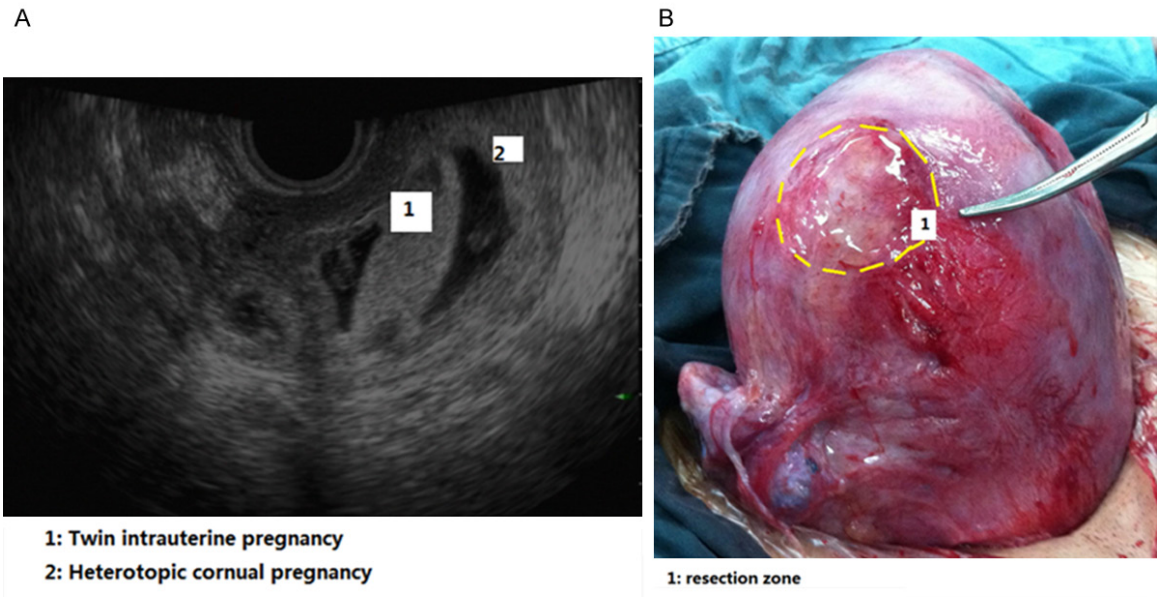


**Figure 1.** A. Ultrasound visualization of the intrauterine twin pregnancy and of the right cornual pregnancy at 6 weeks. B. Appearance of an angular scar zone during the Cesarean section.

by IVF, and the oocytes were frozen to prevent ovarian hyperstimulation syndrome. Frozen-thawed embryo transfer (ET) was planned for the next cycle. Two embryos were transferred at a time and luteal phase support was provided in the form of intravaginal micronized progesterone (P).

The analysis of blood human chorionic gonadotropin (β-hCG) assay was carried out on postoperative days 12 and 23, and the β-hCG levels were 737.4 and 57,732 IU/mL, respectively. The first ultrasound scan performed 24 days after transfer showed a progressive bichorial, biamniotic twin pregnancy.

During the sixth gestational week (by IVF dating), an ultrasound scan showed the persistence of the progressive intrauterine twin pregnancy, combined with a 2.6 × 2.7 × 2.2 $cm^3$ echogenic mass in the right cornu containing a 1.3-cm gestational sac without cardiac activity (**Figure 1A**). Given the hypervascular character of the ectopic pregnancy, it was decided to perform a laparotomy to confirm the diagnosis of right cornual pregnancy and maintain the intrauterine pregnancy with better control of hemostasis.

We sectioned the uterine muscle above the base of the implantation of the cornual pregnancy with an electric lancet, and closed the cornual scar using Vicryl 1™ (Johnson & Johnson) using a figure-of-eight suture. Bleeding during surgery was minimal. The blood β-hCG level had declined to 133,706 IU/mL on postoperative day 1, and the sonography confirmed the absence of cornual pregnancy.

The pregnancy continued with no further complications. At 33 weeks of gestation, the patient experienced abdominal pains with uterine activity, and ultrasonography showed a myometrial thickness of 3.2 mm at the uterine horn. Then, we decided to perform a cesarean section at the onset of labor that allowed the birth of two boys weighing 1950 and 1700 g and both with normal Apgar scores. The examination of the right uterine horn showed a reshaped, well-vascularized scar zone with no sign of prerupture (**Figure 1B**).

*Case report 2*

This 30-year-old nulliparous woman was a patient at our hospital with primary infertility for 3 years. Her prior history included a bilateral salpingectomy by laparoscopy. One cycle of long course of ovarian stimulation was initiated, and 14 of 19 retrieved oocytes were successfully fertilized by IVF. The first IVF did not lead to the development of a pregnancy.

In the next cycle, frozen-thawed ET was planned. After discussion with the couple, it was

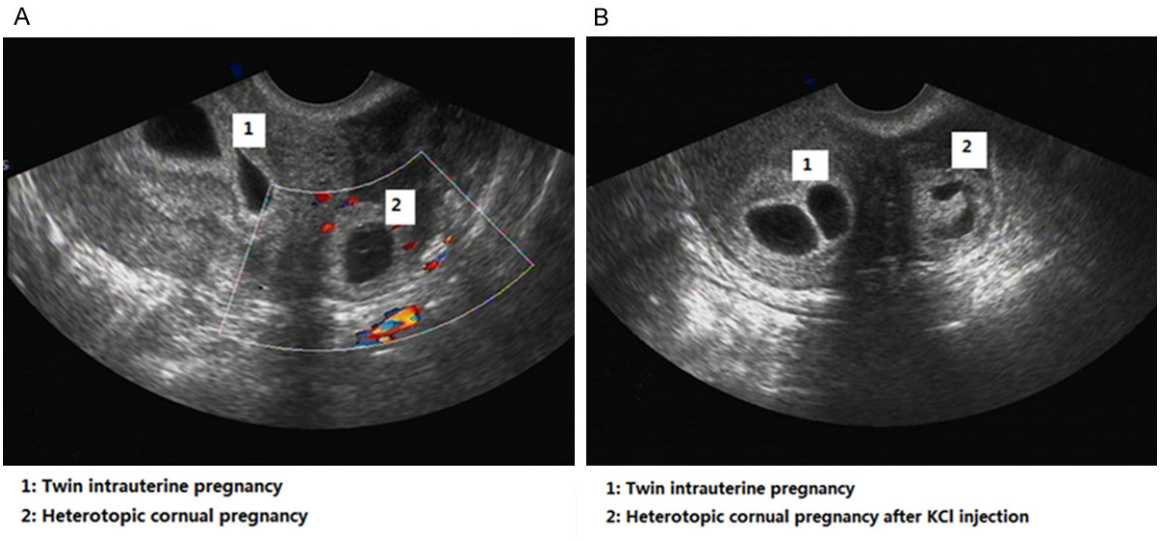


**Figure 2.** A. Ultrasound image of the viable intrauterine twin and of the left cornual pregnancy at 6 weeks. B. Ultrasound confirmation of the left cornual pregnancy on postoperative day 18.

decided to transfer three embryos. The patient received luteal phase support in the form of intravaginal micronized P until the day of the β-hCG assay.

Blood β-hCG assay was carried out on days 13 and 29 after ET and the β-hCG concentrations were found to be 791.8 and 70,064 IU/mL, respectively. In the sixth gestational week (by IVF dating), transvaginal ultrasound scan revealed a heterotopic pregnancy, a viable intrauterine twin pregnancy (embryo bud length, 0.3 mm, with positive fetal heart motion) and a 2.7 × 2.3 × 2.3 $cm^3$ eccentric echogenic mass in the left cornu (containing a 14-mm gestational sac without embryo bud; **Figure 2A**).

As the patient was stable and there was no fluid detected in the cul-de-sac, the heterotopic cornual pregnancy was treated conservatively at 6 weeks and 1 day of gestation (by IVF dating). Under epidural anesthesia, a 17-gauge needle was introduced into the sac using a puncture instrument showing the path to be followed when the needle is inserted (GIP, Wilson-Cook). After the celomic fluid was aspirated, the left cornu was directly injected with 1 mL of 10% KCl guided by transvaginal sonography.

Transvaginal sonography carried out on postoperative day 1 confirmed the absence of cornual pregnancy, and the mass in the left cornu could still be visualized with hypervascularization. A small amount of fluid collection could be observed in the pelvic cavity. The blood β-hCG concentration had declined to 85,626 IU/mL. The patient was discharged on postoperative day 6 without any complication. Transvaginal sonography 2 weeks after surgery revealed continued normal growth of the intrauterine pregnancy without signs of uterine rupture, and the corneal pregnancy was not growing (**Figure 2B**).

At 35 weeks of gestation, the patient was admitted for severe preeclampsia. Before the admission, she had received routine therapies at a local hospital (magnesium sulfate, full-dose antihypertensive medication, and dexamethasone for fetal lung maturity), but failed to respond to the medication. After informed written consent was obtained, a Cesarean section was performed. She delivered two healthy babies, a boy and a girl weighing 2,200 and 1,900 g, respectively, both with Apgar scores of 10 at 1 and 5 minutes.

## Discussion

Heterotopic triplet pregnancy is an exceptional occurrence in natural pregnancies, and its possible risk factors include past pelvic inflammatory disease, previous pelvic surgery, uterine anomalies, peri- and intratubular adhesions, embryonic chromosomal abnormalities, and maternal endocrine factors. Its incidence is

increased after IVF-ET, reaching a rate estimated at around 1%. The risk factors include a high number of transferred embryos, poor embryo quality, and ET techniques such as transfer near the uterine horn or excessive pressure on the syringe during transfer [4]. And the embryo quality, patient age (<35 years), pelvic condition, and the hormonal milieu are also possible causes [5]. The American Society of Reproductive Medicine guidelines recommend limiting the transfer to two good-quality embryos for a young woman. Although fewer embryos are transferred in an IVF-ET cycle in order to minimize multiple pregnancies, consideration may be given to the transfer of more than the recommended number of embryos in subsequent IVF-ET cycles in women with poor prognoses who have had multiple failed fresh IVF-ET cycles [6]. In the two cases reported here, previous uni- or bilateral salpingectomy was a major predisposing factor of the heterotopic pregnancy. The other factor was the age of the patient (<35 years). The second patient had failed her first cycle of IVF before; therefore, we decided to transfer three embryos.

The accurate diagnosis of heterotopic pregnancy is a challenge due to the diverse locations at which an ectopic pregnancy can implant. The typical symptoms include abdominal pain, adnexal mass, peritoneal irritation, and enlarged uterus, but more than half of the patients with a heterotopic pregnancy may be asymptomatic. β-hCG detection assays and ultrasound diagnosis have allowed more frequent detection of interstitial pregnancies before the rise of clinical symptoms and signs. In our cases, both the patients showed no symptoms and received routine β-hCG testing and transvaginal ultrasound examination to confirm the presence of a pregnancy. The diagnosis in both cases was made by ultrasound scans showing a cornual pregnancy containing a gestational sac combined with a intrauterine twin pregnancy at approximately the sixth week of gestation (by IVF dating).

In the published work, there are several treatments for ectopic pregnancy [7], including surgical excision by laparotomy or laparoscopy and medical treatment with locally injected KCl or methotrexate. Although the management remains controversial, it is still vital to achieve an early diagnosis and treatment in accordance with these conditions is still vital. In the cases we encountered here, ectopic pregnancy in the uterine horn faced a high risk of rupture and hemorrhage because of the voluminous and hypervascular character of cornual mass supplied by the branches of the uterine and ovarian arteries. However, conventional management is not recommended due to its unclear impact on patient morbidity and risk of uterine rupture.

The most frequently described treatment is surgical, by resection of the uterine horn by laparotomy or laparoscopy. The rate of live births is around 40% [8]. The choice of laparotomy seemed more reliable to us than laparoscopy, to ensure a solid myometrial suture, as well as a perfect hemostasis. Laparotomy can provide several advantages, including excellent operative field exposure, less mechanical stimulation to the uterus, and reduced hospital stay. In a previous systematic review, the split between laparoscopy and laparotomy was 37% and 61%, respectively [2]. Another study reported that laparoscopy was converted to a laparotomy because of hemorrhage [9]. Given the hemodynamic instability in an emergency setting, laparotomy is more effective for controlling hemorrhage and maintaining hemostasis.

The second option for ectopic pregnancy is medical treatment by ultrasound-guided injection of KCl or a hyperosmolar solution in situ, rarely combined with methotrexate because of its toxicity [10]. This method is ideal for a heterotopic pregnancy containing embryos with cardiac activity [11] and does not render the uterus more fragile. However, there are several major difficulties encountered in managing such cases. First, it creates a risk of hemorrhage related to rupture because of the elevated serum β-hCG levels along with the progression of the intrauterine gestation [6, 8]. Ultrasound surveillance must be followed up closely to make sure that the ectopic gestation is not growing and there are no signs of uterine rupture. Second, introducing the needle into the myometrium of the uterine horn may induce uterine contractions; therefore, the procedure should be performed by a senior surgeon to minimize the mechanical trauma. However, some studies have reported abortion of intrauterine gestation in cases of heterotopic corneal pregnancies that were treated with local

injection of KCl [12], and the success rate of the operation and pregnancy outcome of the intrauterine pregnancy are the same as those obtained with surgical treatment [13].

The final pregnancy outcome depends on the development of the intrauterine pregnancy and the management of ectopic gestation. The survival rate of heterotopic pregnancy was 69% in 2007 [14] and 66% in 2011 [2], but cornual heterotopic pregnancies are too rare to seriously consider. Several factors decided the deliver such as gestational age, position of the fetuses, the ease of fetal heart rate monitoring, and the maternal and fetal status. Cesarean sections were performed for both the cases in urgency at the onset of labor to avoid possible uterine rupture in the first case and because severe preeclampsia was diagnosed with immature cervical status at 35 weeks of gestation in the second case. Although there is no universal consensus in this regard, evidence suggests that women with a history of cornual resection have increased maternal and perinatal morbidity associated with vaginal birth.

In conclusion, the incidence of a heterotopic pregnancy dramatically increases after IVF-ET, particularly in patients with risk factors. Nevertheless, it is essential to remain vigilant in order to diagnose the occurrence as soon as possible if associated symptoms appear. Management of heterotopic pregnancy should focus on removal of the ectopic gestation and preserving the life of both the mother and the intrauterine pregnancy. As both surgical and conservative treatment require close follow-up and favorable pregnancy outcomes can be attained, large randomized trials are vital to determine the risk and benefit of the management of this condition.

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## Disclosure of conflict of interest

None.

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