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Heterotopic triplet pregnancy: report of a patient with remnant tubal ectopic and intrauterine twin pregnancy after frozen-thawed embryo transfer

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Abstract
A case of heterotopic triplet pregnancy after frozen-thawed embryo transfer is presented. The patient conceived after transfer of three frozen-thawed embryos at a fertility clinic where she had previously undergone laparoscopic left salpingectomy due to pyosalpinx. Approximately 4 weeks after the embryo transfer, she presented with a complaint of abnormal genital bleeding and was diagnosed as having a dichorionic twin pregnancy by ultrasound. One week later, she was referred to our hospital because of lower abdominal pain. Hematoperitoneum was suspected based on findings of low blood pressure and tachycardia. Diagnostic emergent laparoscopy demonstrated an ectopic pregnancy in the remnant isthmic portion of the left tube. Laparoscopic excision of the remnant fallopian tube was performed, but the procedure resulted in early pregnant loss of one of the twins. The risk of heterotopic pregnancy is not small under assisted reproductive technology. Attention should be paid to the risk of tubal pregnancy after transferring more than two embryos or controlled ovarian hyperstimulation even after salpingectomy had been performed.

Key words: heterotopic pregnancy, in vitro fertilization and embryo transfer, laparoscopic surgery, remnant fallopian tube
Introduction

Heterotopic pregnancy (HP) is the coexistence of a pregnancy with intrauterine development and at least one ectopic pregnancy at any site. The incidence of HP in natural conception is low, occurring in one of 30,000 pregnancies [1-3], but the incidence of HP rises to 1 in every 100 pregnancies conceived by in vitro fertilization and embryo transfer (IVF-ET) [4, 5]. The increased incidence of HP is a serious problem, as the diagnosis of this condition is quite difficult and the management of HP is challenging.

Here we present a case of heterotopic triplet pregnancy with isthmic implantation in the left remnant tube and intrauterine twin pregnancy after frozen-thawed embryo transfer. Surgical treatment of the isthmic portion of the left remnant tubal pregnancy resulted in the birth of a healthy girl. To our knowledge, this is the first report of a case of heterotopic triplet pregnancy with ectopic site occurring in the remnant tube after ipsilateral salpingectomy.

Case report

A 31-year-old woman (gravida 2, para 0) with a 6-year history of infertility consulted a private clinic for evaluation. Diagnostic laparoscopy demonstrated left pyosalpinx with right tubal obstruction due to bilateral adnexal adhesion. She underwent a laparoscopic left salpingectomy and IVF-ET was initiated. After the second cycle of frozen-thawed ET in which 3 embryos were transferred, she became pregnant. At 6 weeks of pregnancy, the patient again consulted the private clinic due to abnormal genital bleeding. An ultrasound scan showed an ongoing dichorionic twin pregnancy. A diagnosis of threatened abortion was made, and she was admitted to that clinic. Seven days later the patient started to complain of lower abdominal pain that gradually worsened. Ultrasound examination on the 7th day of admission demonstrated viable intrauterine twin pregnancy and the presence of free fluid in the pouch of Douglas. As rupture of an ectopic pregnancy was suspected, she was transferred to Kumamoto University Hospital. On admission, she appeared pale with cold extremities in a pre-shock state. Pulse rate was 100/min and blood pressure was 70/50 mmHg. Physical examination demonstrated diffuse abdominal tenderness. Hemoglobin was 9.2 g/dl, white blood cell count
14,900/µl and serum hCG was 158,269.0 mIU/ml. She was transferred to the operating room and an emergency laparoscopy was performed at 7 weeks 4 days of gestation.

At laparoscopic surgery, intraabdominal hemorrhage and pelvic adhesion were observed. At least 2,300ml of peritoneal blood was evacuated, 600ml of which was returned to the patient using Cell Saver®. As the patient had undergone left salpingectomy previously, we first explored the right tube for the ectopic implantation site but no mass was found in the right tube. We next examined the left uterine cornu. The muscle layer of the left cornu was normal, but bleeding from the isthmic portion of the truncated left tube was observed. After excluding interstitial pregnancy by intraoperative transvaginal ultrasound, rupture of the isthmic portion was confirmed and a piece of free tissue was recovered from the isthmic portion of the left tube (Fig. 1). Laparoscopic excision of the ruptured left isthmic portion was carried out using a Harmonic Scalpel®. The two-layer closure of the left isthmic portion was then performed. The deeper layer of myometrium was closed with 3-0 Vicryl® suture. The superficial layer was closed with 2-0 Vicryl® suture (Fig. 2). Histopathological examination confirmed the presence of chorionic villous tissue attached to the muscle layer. On the 4th postoperative day (8 weeks 1 day of gestation), fetal death of one of the twins near the left uterine cornu was confirmed (Fig. 3). The patient was discharged on the twenty-second day postoperatively. Obstetric follow-up was normal and showed good fetal growth. Magnetic resonance imaging of the pelvis performed at 33 weeks of pregnancy did not demonstrate any signs indicating threatened rupture of the uterus. By elective cesarean section at 37 weeks of gestation because of the prior possible cornual resection, the patient gave birth to a female baby weighed 2,828g with Apgar scores of 8 and 9 at 1 and 5 min, respectively. No muscle layer defect in the left isthmic portion was found at cesarean section (Fig. 4).

Discussion

HP is a rare and potentially fatal condition with an incidence of one in 30,000 for spontaneous conception and one in 100 for assisted reproductive technology (ART). Heterotopic triplets are even more rare and cases demonstrating tubal ectopic and coexisting twin intrauterine pregnancy are limited to only 15 cases in the literature [6].

As tubal pregnancy at an isthmic portion is a rare event, it is clear that the implantation inside a remnant tube is less common [7]. Risk factors for remnant tubal pregnancy
include salpingectomy for hydrosalpinx, as such procedures cannot excise the patent corneal and intramural segment of the damaged tube [8]. Transfer depth might be another risk factor for ectopic pregnancy [9]. Thus, even if a complete salpingectomy was performed, attention should be paid for the possibility of remnant tubal pregnancy. In our case, prior salpingectomy for hydrosalpinx, the number of embryos replaced and the transfer depth might be potentially responsible for the remnant tubal implantation.

The diagnosis of HP is difficult because it tends to be overlooked after confirming the intrauterine pregnancy by transvaginal ultrasound. It is even more difficult in cases of controlled ovarian hyperstimulation (COH) as the ovaries are enlarged with multiple luteal cysts. In our case, exploratory laparoscopy was indicated in order to confirm the diagnosis. After ruling out interstitial pregnancy by intraoperative transvaginal ultrasound, excision of the ruptured left isthmic portion of the remnant tube after ipsilateral salpingectomy was performed under laparoscopy.

Though long-term effects of laparoscopic surgery during pregnancy on the child after birth have not been well studied [10], the numbers of laparoscopic treatment in gravid patients such as cholecystectomy, ovarian cystectomy and HP have been increasing and the safety of these procedures has been well documented [11]. The patient experienced single fetal demise of one twin near the left cornu. As the uterine cornu has an abundant blood supply from branches of the ovarian and uterine arteries, the bleeding near the left corneal portion might have had some adverse effect to the embryo near the left cornu.

Conservative treatment by locally injecting potassium chloride or methotrexate is an option in HP especially in cases involving cervical pregnancy [12]. Few cases undergoing conservative treatment of HP have been reported in the literature because of concern regarding toxicity to the fetus [13]. Most cases of HP with tubal pregnancy have been treated surgically [11].

We encountered this case before the Japan Society of Obstetrics and Gynecology and Japan Society for Reproductive Medicine revised the guidelines in 2008 regarding limits on the number of embryos to be transferred [14]. The single embryo transfer policy acts not only to reduce multiple pregnancies but also to prevent HP in IVF-ET cycles. The risk of HP remains in patients receiving non-ART COH regimens.

In conclusion, when pregnancy is achieved after transferring more than two embryos or after COH, the adnexae should be carefully examined by transvaginal ultrasonography early in gestation, even after salpingectomy had been performed or
even if an intrauterine gestational sac is already confirmed. Although the diagnosis of HP remains a challenging problem, we could preserve one of the intrauterine pregnancies of heterotopic triplet by surgically excising the ectopic gestation in the tubal remnant.
References


Figure legends

Figure 1
(A) Findings of the ruptured isthmic portion of the left remnant tube (arrow) with hematoperitoneum during laparoscopic surgery. (B) A piece of free tissue (arrow) was recovered from the ruptured isthmic portion of the left remnant tube.

Figure 2
Intraoperative macroscopic view of the left uterine cornu during laparoscopic surgery for ectopic pregnancy. The left isthmic portion was closed with two-layer suture.

Figure 3
Vaginal ultrasonography of the uterus showed intrauterine dichorionic twin pregnancy with (arrow) and without (arrow head) cardiac activity on the fourth postoperative day.

Figure 4
Intraoperative macroscopic view of the left uterine cornu during Caesarean section. No muscle layer defect in the left isthmic portion was found.