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**Heterotopic Intrauterine and Cervical Pregnancy:  
Case Report and Literature Review**

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**Abstract**

**Objective:** Heterotopic intrauterine and cervical pregnancy is a rare but life-threatening gynecological condition. Given that there are no protocols for the management of heterotopic intrauterine and cervical pregnancy due to its rarity, we presented our three cases of heterotopic intrauterine and cervical pregnancy, and further conducted a literature review, aiming to figure out the most effective treatment approach.

**Case Report:** Both case 1 and 2 underwent surgical removal of both intrauterine and cervical pregnancies after prior uterine artery embolization, while case 3 underwent cervical pregnancy reduction by manual forceps evacuation, and a healthy male baby weighing 3350 g was delivered by elective cesarean section at 39+3 weeks of gestation. For all the three cases, no significant post-operative adverse events were found.

**Conclusion:** Individualized surgical approach based on the patient's condition is the preferred treatment for patients with heterotopic intrauterine and cervical pregnancy.

**Introduction**

Cervical pregnancy is rare in pregnancies with an occurrence of 1:1,000-95,000, representing less than 1% of all ectopic pregnancies[1]. Misdiagnosis or improper handling of cervical pregnancy can result in hemorrhagic shock, which requires hysterectomy or arterial embolization to save patients' lives. Twin pregnancies contribute to 3% of the births while experiencing more morbidity and mortality than singleton pregnancies[2]. Twin pregnancy of cervical pregnancy and intrauterine pregnancy is rarely reported and easily misdiagnosed, making it difficult for clinicians to figure out a more satisfactory and safer treatment. Currently, there are no clinical guidelines for heterotopic intrauterine and cervical pregnancy.

In this case report, we present three cases of heterotopic intrauterine and cervical pregnancy, one by spontaneous fertilization, two by assisted reproductive technology in-vitro fertilization and embryo transfer (IVF-ET). We aim to figure out the indications for pregnancy-preserving treatment and provide experiences for clinicians through our cases to maximize the benefits of patients.

## Case Presentation

### Case 1

A 25-year-old woman, gravida 4, para 2, who was pregnant at 6+5 weeks of gestation by her last menstrual period, presented to our emergency department, complained of a 10-day history of vaginal spotting and mild lower abdominal pain, denied suffering from dizziness or morning sickness. A small amount of vaginal bleeding had developed few hours before the emergency visit. Her gynecological history was unremarkable, with a normal previous menstrual cycle. Her obstetric history included a vaginal delivery 5 years ago, a cesarean section due to the vasa previa 2 years ago, and an induced abortion by vacuum aspiration in the first-trimester. This pregnancy was a natural conception without previously fertility treatment.

Pelvic examination revealed a small amount of blood in the vagina, cervical motion tenderness, and an enlarged softened uterus, while no abnormalities in the adnexal areas.

The laboratory examination revealed the serum beta-human chorionic gonadotropin ( $\beta$ -hCG) of 30423.92 IU/L. Transvaginal ultrasound examination revealed two visible gestational sacs (Fig. 1A-D), detailed information as shown in Table 1.

With the clinical manifestations, the  $\beta$ -hCG level and the ultrasound examination result, the heterotopic intrauterine and cervical pregnancy was considered as the diagnosis. Surgical termination of pregnancy was established according the patient's requirement. To prevent life-threatening haemorrhage during the surgery, prior uterine artery embolization was carried out using the granular gelfoam, and 50 mg of methotrexate (MTX) was injected in the cervix. Hysteroscopic resection was performed 2 days later to remove both the intrauterine and cervical pregnancy. Postoperatively, 10 IU of oxytocin was injected into the cervix to facilitate hemostasis. The operation was successful. Histopathological examination results verified the decidua and chorion in excision (Fig. 1E-H). Her  $\beta$ -hCG levels were 35922.09 IU/L and 4244.61 IU/L respectively 1 day before and 1 day after the operation. The patient had a well off recovery, postoperative condition is described in Supplemental Material (Section: Case 1 - General information & Treatment - Outcome).

### Case 2

A 39-year-old woman, gravida 3, abortion 2, presented to our center with amenorrhea for 45 days, vaginal bleeding and mild lower abdominal pain for 4 days. She had a history of IVF with two embryos transferred 28 days ago for her primary infertility. Her gynecological history included an

abdominal myomectomy 12 years ago and a diagnostic curettage for endometrial polyp last year. Her obstetric history included two spontaneous abortions during early pregnancy. Her blood group was Rhesus B negative.

On speculum examination, about 300 ml of blood was found in the vagina, and the appearance of cervix was normal, with a closed external os.

Laboratory examination revealed the serum  $\beta$ -hCG was 93043.43 IU/L, and the serum progesterone was more than 42.60  $\mu$ g/L. Transvaginal ultrasound examination revealed two visible gestational sacs (Fig. 2A-D), detailed information as shown in Table 1.

With the clinical manifestations, the  $\beta$ -hCG level and the ultrasound examination result, the heterotopic intrauterine and cervical pregnancy was considered as the diagnosis. Uterine artery embolization was performed, followed by an intramuscular injection of 300  $\mu$ g Rho(D) immune globulin. Segmental aspiration of cervix and uterine cavity was then performed 2 days later, followed by an injection of 20 IU oxytocin into the cervix after the aspiration. Operation went smoothly and the histology verified the decidua and chorion in excision (Fig. 2E-H). Her  $\beta$ -hCG was 23856.61 IU/L 1 day after the operation. The patient had a well off recovery, postoperative condition is described in Supplemental Material (Section: Case 2 - General information & Treatment - Outcome).

### Case 3

A 36-year-old woman, gravida 1, presented to our center with amenorrhea for 52 days. She had a history of IVF with two embryos transferred 35 days ago. Her previous menstrual cycle was normal. Both her gynecological and obstetrics history were unremarkable, except primary infertility was indicated.

Transvaginal ultrasound examination revealed two visible gestational sacs (Fig. 3A,B), detailed information as shown in Table 1.

Two days later, she developed vaginal bleeding without obvious cause. On speculum examination, a moderate amount of blood was found in the vagina, and a dilated external os was visualized with a tissue about 1cm $\times$ 2cm incarcerated inside. On laboratory examination, the serum  $\beta$ -hCG was 172621.88 IU/L, and the serum progesterone was more than 42.60  $\mu$ g/L.

With the clinical manifestations, the  $\beta$ -hCG level and the ultrasound examination result, the heterotopic intrauterine and cervical pregnancy was considered as the diagnosis. Selective termination of the cervical pregnancy but preserving the concurrent intrauterine pregnancy

**Table 1:** Sonographic information of the three cases' gestational sacs

	Case 1		Case 2		Case 3	
	Sac 1	Sac 2	Sac 1	Sac 2	Sac 1	Sac 2
Location of implantation	intrauterine	cervical canal	intrauterine	cervical canal, 5 mm from the external os	intrauterine	cervical canal, 12 mm from the external os
Fetal pole	present	present	present	present	present	present
Yolk sac	present	present	present	present	present	present
Cardiac activity	present	faint	present	present	present	present
Size of gestational sac (cm)	1.8×0.9×1.7	0.9×0.6×0.8	1.5×1.0×2.8	1.8×0.9×1.2	2.2×2.9×3.2	1.5×1.5×1.8
Length of CRL (mm)	5	1	5	4	11	2.5
Estimate GA by CRL (weeks)	6 <sup>+1</sup>	5	6 <sup>+1</sup>	6 <sup>+0</sup>	7 <sup>+2</sup>	5 <sup>+6</sup>
Difference between estimate GA by CRL and theoretical GA by LMP (weeks)	-0 <sup>+4</sup>	-1 <sup>+5</sup>	-0 <sup>+2</sup>	-0 <sup>+3</sup>	-0 <sup>+1</sup>	-1 <sup>+4</sup>

**Abbreviation:** CRL: crown-rump length, GA: gestational age, LMP: last menstrual period

was preferred. Manual forceps evacuation of the cervical pregnancy was performed, with the following histology showed the excision included decidua and chorionic villus (Fig. 3C,D). The serum  $\beta$ -hCG levels were 164164.06 IU/L and 172621.88 IU/L respectively 2 days before and 1 day after the evacuation. However, vaginal bleeding persisted and remained no signs of remission 1 week after the surgery, and an abnormal echo in the cervix was revealed by the transvaginal ultrasound examination, suggesting the possibility of the retained materials from the cervical pregnancy. Therefore, 8 days after the first manual forceps evacuation, a second manual forceps evacuation with the aim to remove the persistent trophoblastic materials was carried out. The operation went smoothly and the following histology showed the excision was the residue from the pregnancy (Fig. 3E,F). On laboratory examination, the serum  $\beta$ -hCG levels were 179835 IU/L and 207773.98 IU/L respectively 9 hours before and 4 days after the second evacuation.

The patient had a well-off recovery. The cervical pregnancy was successfully removed with the preservation of the intrauterine embryo. Regular obstetric follow-ups were done for the intrauterine pregnancy, and a healthy male infant weighting 3350 g was delivered by cesarean section at the 39+3 weeks of gestation. Her serum  $\beta$ -hCG had been monitored from 10 days after the ET to 4 days after the second manual forceps evacuation, the trend as shown in Fig. 4.

## Discussion

Currently, no protocols have yet been published on heterotopic intrauterine and cervical pregnancy. Treatment

decision on whether to preserve the intrauterine pregnancy should be based on the patient's wishes, maternal life safety consideration and whether the intrauterine pregnancy can survive.

Provided that the preservation of the intrauterine pregnancy is not required or possible, the focus of treatment is on how to avoid uncontrollable hemorrhage during pregnancy removal. Preoperative uterine artery embolization is the most used approach, as practiced in case 1 and 2. However, ischemia induced by occlusion of uterine artery may cause inflammatory responses and local necrosis[3-5], which in turn poses potentially adverse effects on the endometrium and ovaries. For patients who desire future pregnancies, transvaginal ligation of the cervicovaginal branches of the uterine artery maybe a feasible alternative. Injection of oxytocin into the cervix postoperatively is also a recommended approach to facilitate hemostasis, as practiced in case 1 and 2.

To preserve the intrauterine pregnancy, no conclusions have yet been reached on the best treatment approach to date. Generally, higher serum  $\beta$ -hCG and progesterone levels generally reveal higher viability of the intrauterine embryo[6-8]. Moreover, an intrauterine gestational sac with size that matches the theoretical gestational age, a gestational-age-appropriate CRL, and a fetal pole with cardiac activity visualized on ultrasound examination also suggest a better development embryo, which favor the intrauterine pregnancy preservation.

Literature review of heterotopic intrauterine and cervical pregnancy are presented in Table 2. A variety of treatment approaches of heterotopic intrauterine and

**Table 2:** Review of literature

Article	Age	Pregnancy	Previous medical history	Diagnosis time	Initial hCG level	hCG increasing tendency	Treatment	Adverse event after operation	Outcome	
										Abasiattai (2020) [9]
Kumar (2004) [10]	32	Spontaneous	Gravida 2, Para 1	A cesarean section	7 weeks	Not reported	Not reported	KCl injected into the cervical gestational sac	Impending eclampsia, Profuse hemorrhage from the cervical site during the delivery of	Deliver an infant by cesarean section at 35 weeks
Sierra (2022) [11]	39	IVF-ET	Gravida 3, Para 1	Right salpingectomy	7 <sup>+</sup> weeks	Not reported	Not reported	KCl injected into the cervical gestational sac-aspiration	Intrauterine infant PROM, Profuse hemorrhage from the cervical site during the delivery of Intrauterine infant	Deliver a 1800 g infant by cesarean section at 32 <sup>+</sup> weeks
Sudhakar (2021) [12]	32	IVF / ICSI	Primigravid	Polypectomy, Bilateral tubal block	6 weeks	932 mIU/mL 12 days after ET	+80.3% in 2 days	KCl injected into the cervical gestational sac after intra-amniotic fluid aspirated	Profuse hemorrhage from the cervical site during the delivery of intrauterine infant, resulted in hysterectomy	Deliver a healthy 2.8 kg female infant by cesarean section at 37 weeks
Deka (2012) [13]	36	IVF / ICSI	Gravida 2, Para 0	A spontaneous miscarriage, Bilateral salpingectomy	5 weeks	Not reported	Not reported	KCl injected into the cervical gestational sac after intra-amniotic fluid aspirated	Uneventful	Deliver a healthy 3.0 kg male infant by cesarean section at 38 weeks
Gilbert (2020) [17]	42	Not reported	Gravida 3, Para 0	Not reported	8 weeks and 3 days	Not reported	Not reported	MTX injected into the cervical gestational sac	Uneventful	Term birth of a infant

Protocic (2007) [14]	31	IVF-ET	Gravida 3, Para 0	Bilateral salpingectomy due to two tubal ectopic pregnancies	6 weeks	74.572 U/L	Not reported	Hypertonic solution of sodium chloride injected into the cervical gestational sac after intra-amniotic fluid aspirated	Not reported	Ongoing intrauterine pregnancy
Suzuki (2007) [15]	35	IVF-ET	Primigravid	Not reported	24 days after ET	Not reported	Not reported	Hyperosmolar glucose injected into the cervical gestational sac after intra-amniotic fluid aspirated	PROM, Postpartum vaginal bleeding (ultrasound revealed a large hematoma in the cervical canal)	Deliver a 2102 g male infant and a 1760 g female infant through cesarean section at 34 weeks
Liu (2019) [16]	26	IVF-ET	Primigravid	Chronic salpingitis, Left tubal obstruction	7 weeks	742.47 mIU/mL 14 days after ET	Not reported	Absolute ethanol injected into the cervical gestational sac	Uneventful	Vaginally deliver a 1500 g male infant at 30 weeks
Bhairavi (2019) [18]	31	IVF-ET	Not reported	Bilateral salpingectomy	6 weeks	Not reported	Not reported	Cervical gestational sac aspiration	Uneventful	Deliver a 3.2 kg male infant by cesarean section at 37 weeks
Faschin gbauer (2011) [19]	25	Ovulation induction	Primigravid	Primary infertility	9 weeks	Not reported	Not reported	Cervical gestational sac aspiration	PROM	Vaginally deliver a 3150 g newborn at 39 <sup>3</sup> weeks
Tsakos (2015) [20]	41	IVF	Gravida 2, Para 0	Premature ovarian failure, Ectopic cervical pregnancy	5 weeks and 3 days	172 mIU/mL 9 days after ET	+142.7% in 2 days	Cervical gestational sac aspiration	Not reported	Deliver a 2900 g female infant through cesarean section at 38 weeks
Fan (2022) [21]	29	IVF/CSI	Primigravid	Unremarkable	42 days after ET	819 mIU/mL 2 weeks after ET	Not reported	Cervical gestational sac aspiration	Uneventful	Deliver a 2750 g female infant through cesarean section at 39 weeks
Correa (2022) [22]	41	IVF-ET	Primigravid	Diminished ovarian reserve	26 days after ET	355 mIU/mL 10 days after ET	Not reported	Aspiration+curetage of cervical gestational sac	Painless vaginal bleeding after operation	Deliver a healthy 2960 g female infant through cesarean section at 37 weeks
Terra (2019) [23]	39	IVF-ET	Gravida 6, Para 0	Five spontaneous abortions, Hysteroscopic myomectomy, Secondary infertility	7 <sup>5</sup> weeks	Not reported	Not reported	Cervical curettage	Uneventful	Deliver a 3215 g infant by cesarean section at 39 weeks

Saito (2017) [24]	39	IVF-ET	Gravida 7, Para 3	Spontaneous and artificial abortions, Salpingectomy due to ectopic pregnancy	5 <sup>-2</sup> weeks	Not reported	Not reported	Manual forceps evacuation of cervical gestational sac	Vasa previa, Total placenta accreta of Intrauterine pregnancy resulted in hysterectomy	Deliver a healthy female infant through cesarean section at 36 weeks
Kim (2012) [25]	36	IVF/ICSI	Gravida 2, Para 0	Dilation & curettage due to a missed abortion, Multiple uterine fibroids	4 <sup>-5</sup> weeks	191.44 mIU/mL 11 days after ET	+704.4% in 4 days	Manual forceps evacuation of cervical gestational sac	Uneventful	Deliver a 3360 g infant through cesarean section at 40 <sup>-5</sup> weeks
Rubattu (2020) [26]	32	IVF/ICSI	Primigravid	Male factor infertility	3 weeks after ET	462 mIU/mL 13 days after ET	+671.2% in 4 days	Hysteroscopic resection of cervical gestational sac	Uneventful	Deliver a 2900 g female infant through cesarean section at 39 weeks
Jozwiak (2003) [27]	37	IVF/ICSI	Primigravid	Primary infertility	25 days after ET	64 mIU/mL 12 days after ET	+137.5% in 1 day	Hysteroscopic resection of cervical gestational sac	Minor vaginal bleeding after resection	Deliver a 3050 g female infant through cesarean section at 38 weeks
Schivardi (2020) [28]	36	IVF-ET	Primigravid	Tubal infertility	5 <sup>-5</sup> weeks	Not reported	Not reported	Microwave ablation of cervical gestational sac	Profuse vaginal bleeding with irregular uterine contractions at 37 <sup>-6</sup> weeks	Deliver a 2780 g female infant through cesarean section at 37 <sup>-6</sup> weeks
Sepúlveda (2020) [29]	36	Ovulation induction+IUI	Primigravid	Primary infertility due to azoospermia (male factor)	7 <sup>-4</sup> weeks	Not reported	Not reported	Laser ablation of cervical gestational sac	Uneventful	Deliver a 2670 g male infant through cesarean section at 36 weeks

**Abbreviation:** ET: embryo transfer, hCG: human chorionic gonadotropin, ICSI: intracytoplasmic sperm injection, IUI: intrauterine insemination, IVF: in vitro fertilization, KCI: potassium chloride, PROM: premature rupture of membrane

cervical pregnancy had been described in the literature, which can be classified mainly into pharmacological and surgical treatment.

Pharmacological treatment appears to be the most commonly used method for selective termination of cervical pregnancy from the existing case reports. Common methods include injection of potassium chloride[9-13], high-concentration sodium chloride[14], hyperosmolar glucose[15] or absolute ethanol[16] into the ectopic embryo sac under ultrasound guidance. Although there had also been reports[13,17]of methotrexate used, it is not recommended as local absorption into the blood may still have teratogenic effect on the persistent intrauterine embryo. Although pharmacological treatment has the advantage of being less invasive, complications such as long-term ectopic pregnancy mass rupture[10-13,15], local infection and subsequent intrauterine infection may occur due to the unabsorbed tissue from the cervical pregnancy. Therefore, pharmacological treatment is not yet a satisfactory treatment approach.

Surgical treatment is a more effective approach for heterotopic intrauterine and cervical pregnancy. Common surgical methods include vacuum aspiration[18,22], curettage[22,23], manual forceps evacuation[24,25], hysteroscopic resection[26,27], etc.[28,29] However, no specific surgical method can be recognized as the best. At the earliest stages of cervical pregnancy, especially when the cervical sac is still a fluid sonolucent area in sonography, vacuum aspiration is an ideal method as it poses only little mechanical stimulation to the cervix. When the cervical sac develops and becomes larger, curettage is a more feasible method to resolve the cervical pregnancy; hysteroscopic resection is also an ideal method, with the advantages of direct vision and thorough removal of cervical pregnancy, but these two methods may pose greater mechanical stimulation to the cervix. When the cervical sac becomes much larger or the implantation site of the cervical sac is low enough to cause spontaneous opening of the external cervical os, manual forceps evacuation is preferential. In case 3, the external cervical os had opened, and the cervical sac could be seen through the external os. Therefore, manual forceps evacuation, as a direct, economical method, and most importantly, the method that could induce the least stimulation to the uterus in this situation, was the best treatment option. Our experience also suggests that the presence of retained trophoblast materials may lead to persistent vaginal bleeding, which requires prompt examination and treatment. Uterine artery embolization is not suitable for hemostasis in pregnancy-preserving treatment as ionizing radiation emitted during angiography may affect the intrauterine pregnancy. In addition, progesterone and uterine contraction inhibitors can be used

to support the intrauterine pregnancy after the removal of cervical pregnancy.

Previous study[30] suggested that surgical treatment does not increase the miscarriage rate, it is the timing of treatment that affects the live birth rate. In our opinion, treatment at an earlier gestational age reduces the needs of invasive procedure, thereby reduces the risk of uterine contractions and subsequent miscarriage of the intrauterine pregnancy. Hence, the importance of ultrasound and serum  $\beta$ -hCG examination should be emphasized. An accurate and early diagnosis based on ultrasound and serum  $\beta$ -hCG can prompt treatment to increase the possibility of preserving the concurrent intrauterine pregnancy.

In conclusion, surgical removal of cervical pregnancy is preferred for heterotopic intrauterine and cervical pregnancy patients who wish to preserve the intrauterine pregnancy, but patient-based risk balance is required.

## Statements & Declarations

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The authors have no conflicts of interest relevant to this article.

### Ethics Approval and Consent to Participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Sun Yat-sen Memorial Hospital of Sun Yat-sen University (2023.02.01/No SYSKY-2023-078-01). Informed consent was obtained from all individual participants included in the study.

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