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# Interstitial heterotopic pregnancy after bilateral total salpingectomy in IVF patients: a case report and literature review

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#### **REVIEW PAPER / OBSTETRICS**

## Interstitial heterotopic pregnancy after bilateral total salpingectomy in IVF patients: a case report and literature review

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#### Abstract

**Objectives:** Heterotopic pregnancy of an intrauterine pregnancy and an interstitial or stump pregnancy after bilateral salpingectomy is a rare complication of in vitro fertilization (IVF) that can lead to severe hemorrhage; prompt identification and management are important.

The aim of this paper was to present a case report and an updated literature review of women who had had combined interstitial/stump and intrauterine pregnancies during an in an IVF cycle after total bilateral salpingectomy.

**Material and methods**: We conducted a search in PubMed for reported heterotopic pregnancy, of a combined intrauterine pregnancy with an interstitial or stump pregnancy, in women who underwent IVF after bilateral salpingectomy.

**Results:** Our search yielded 13 heterotopic pregnancies in women who underwent IVF after bilateral salpingectomy. Forty-six percent of the women had more than two embryos transferred, and all the women had a history of ectopic pregnancies or tubal infertility. Most of the women presented at 6–7 weeks of pregnancy with vaginal bleeding and/or abdominal pain. A ruptured ectopic pregnancy was presented in 42%. Ultrasound was the main diagnostic tool in most cases. Only two women had been medically treated with local KCL or methotrexate, while 83% underwent surgical treatment. Five women had uncomplicated cesarean sections near or at term.

**Conclusions**: Women with bilateral total salpingectomy remain at risk of heterotopic pregnancy, which poses a diagnostic and treatment challenge. This risk may be reduced by the reduction in the number of transferred embryos in IVF. For those who

wish to preserve intrauterine pregnancy, cornual resection can be performed with good prognosis.

**Keywords:** interstitial heterotopic pregnancy; bilateral tubal salpingectomy; *in vitro* fertilization; ultrasound; cornual resection

#### INTRODUCTION

Heterotopic pregnancy (HP) is a rare event and occurs in 1 of 7000 pregnancies in the general population [1]. The more frequent use of artificial reproductive technologies has increased the incidence of HP, to 1% in pregnancies after *in vitro* fertilization (IVF) [2]. HP refers to the presence of simultaneous pregnancies at two implantation sites: usually an intrauterine and an extrauterine pregnancy [3]. In clinical practice, timely diagnosis of HP is often challenging due to many cases being asymptomatic or obscured by enlarged ovaries post-ovulation induction. Although the fallopian tubal site is the most common location for HP, other sites such as cornual, cervical or abdominal have also been documented [3]. Hence, a high level of suspicion should be maintained for HP especially in patients undergoing IVF with multiple embryo transfers or ovulation induction. Post-salpingectomy HP poses a rare but challenging scenario. Only a few reports exist in the literature documenting interstitial or stump HP in women who have undergone IVF following bilateral salpingectomy. Given the rich vascularization of the interstitial portion, post-salpingectomy interstitial HP presents a high risk of sudden rupture and severe hemorrhage. Therefore, in patients following tubal sterilization, the potential for heterotopic pregnancy should not be disregarded, even in the presence of viable intrauterine pregnancies. Upon diagnosis of HP, the optimal treatment should be deliberated [4]. The choice of therapeutic approach depends on various factors, with the preservation of the coexisting intrauterine pregnancy being paramount [2]. In 1996, Benfila et al. [4] reported the first case of interstitial HP in a woman undergoing IVF following bilateral salpingectomy. The patient had previously undergone bilateral salpingectomy due to a history of tubal ectopic pregnancy. Subsequently, she underwent an IVF procedure, during which three embryos were transferred. At 7 weeks of pregnancy, an interstitial pregnancy was diagnosed alongside a viable intrauterine pregnancy. Despite treatment with a local KCL injection, unfortunately, the intrauterine pregnancy did not survive.

This report describes one woman with interstitial HP treated at our center, who was treated first by ultrasound (US)-guided aspiration, which was followed by laparoscopic cornual resection using endoloop ligation. We provide an updated review of the literature on women with combined interstitial or stump and intrauterine IVF pregnancies after total bilateral salpingectomy.

#### CASE REPORT

A 35-year-old woman presented to our department complaining of pain in the left lower abdominal quadrant at 5w + 3d of her fourth pregnancy. In IVF treatment, four fresh embryos were transferred 3 weeks earlier. She had no additional symptoms, such as vaginal bleeding or dizziness.

The patient had an obstetric history of three ectopic pregnancies (EUP). Her first pregnancy was achieved through IVF and a right EUP was diagnosed and followed by right salpingectomy. Her second pregnancy was also achieved by IVF, and she underwent left salpingectomy due to an EUP. In her third pregnancy, an EUP was diagnosed in the right tubal stump, and she underwent laparoscopic stump resection.

At admission, a US examination revealed a viable intrauterine pregnancy and a left interstitial pregnancy with a gestational sac (GS) of 6 mm. Several options were offered to the patient including termination of both pregnancies or local injection and surgical resection of the interstitial pregnancy. Under US-guidance, transabdominal aspiration was performed for the interstitial pregnancy to prevent the need for major surgery, ensuring the preservation of the intrauterine pregnancy (Fig. 1). The pathological results of the aspired tissue revealed chorionic villi. During her follow-up examination 7 days later, a repeated US exam showed a hyperechogenic mass of 15.8 mm diameter in the left uterine cornua, with a synchronous intrauterine viable pregnancy. Two weeks later she was re-admitted due to enlargement of the left interstitial pregnancy mass to 32\*37 mm (Fig. 2). Intrauterine pregnancy was viable with a fetus of 26.9 mm crown rump length.

During her hospital stay, our patient complained of diffuse abdominal pain. A US examination revealed a small amount of fluid in the cul-de-sac. Although she had stable vital signs and a normal hemoglobin level, an emergency laparoscopy was performed due to worsening abdominal pain. After suction of blood clots and hemoperitoneum (about 200 mL), a ruptured interstitial pregnancy within the left

salpingectomy site was confirmed. We performed a successful left cornual resection using endoloop ligation.

The pathological report confirmed the presence of trophoblastic tissue in the interstitial portion. She had an uncomplicated post-operative course. The intrauterine pregnancy continued with no complications and with appropriate growth of the fetus. A healthy baby was delivered by elective caesarean section at 37 weeks, weighing 3280 grams and with an Apgar score of 10/10.

**Figure 1.** (a) Left interstitial pregnancy with gestational sac and yolk sac before aspiration and (b) immediately after aspiration



Figure 1a



**Figure 2**. Enlargement of the left interstitial pregnancy mass to 32\*37 mm after initial treatment by aspira aspiration



Figure 2

Material and methods

We searched PubMed for reported cases of HP, of a combined intrauterine pregnancy with an interstitial or stump pregnancy, in women who were being treated by IVF after bilateral salpingectomy. The search criteria included English full text articles published between January 1, 1980, and February 20, 2022, using the following combinations: "interstitial pregnancy", "heterotopic pregnancy", "tubal stump pregnancy", and "bilateral salpingectomy". We manually searched for references of reports and review articles for relevant case reports. Angular or cornual pregnancies were not included. All relevant reports of heterotopic interstitial or tubal stump pregnancies were selected, regardless of management or outcome. Data regarding maternal characteristics, clinical presentation, treatment of HP, and pregnancy outcomes were extracted.

#### RESULTS

The assessment and selection processes of the search are shown in Figure 3. The search yielded 13 relevant case reports, as presented in Table 1 [6–12].

**Table 1.** Data of all the reported patients (including our patient) of heterotopic pregnancy (intrauterine pregnancy combined with interstitial pregnancy or tubal stump pregnancy) following bilateral total salpingectomy in women who were being treated by vitro fertilization

Cas e	Referen ce	Y e	Mat erna	Causes of	No. of	Gestat ional	Sympto ms	Ultrason ographic findings	Treatm ent	Intraute rine
mb er		r r	1 age	ectomy	erred embr	presen tation		munigs		cy outcom
1	Patient describ ed in this case report	2 0 1 4	35	EUP	4	5w + 3d	LT lower abdomi nal pain	LT interstitia l pregnanc y with GS and yolk sac	US- guided aspirati on Laparo scopic LT	Uncom plicated elective CS 37w Birthwe ight - 3280
1	Benifla et al [4]	1 9 9 6	32	EUP	3	7w	Vaginal bleedin g	Interstitia l pregnanc y	Local KCL	Missed abortion
3	Dumesi c et al. [5]	2 0 0 1	37	Hydros alpinx	4	6w	LT lower abdomi nal pain	Viable IUP LT 2 cm mass	LT cornua l resecti on	Missed abortion 13w (trisomy

4	Chang	2	31	EUP	3	7w	Painles	LT MC-	Laparo	CS at
	[6]	0			Day		vaginal	interstitia	resecti	Footling
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					yos		5	y	intersti	first
								Introutori	tial	twin
								ne MC-	ncy	
5	Blazar	2	31	Ovarian	2	6w		Viable	Laparo	Uncom
	[7]	0		hydrosa	Day			IUF		elective
		7		lpinx	3 embr				LT Cornua	CS 37w
6	Paradis	s 2	38	PID		26w	Abdom	LT	Laparo	Classica
	[8]					(Two	pain	interstitia	tomy	during
		5				previo		l	2	laparoto
						admis		y	PRBCs	iiiy
						sions				
						abdo				
7	Wu et	2				6w	Vaginal	Viable	Local	
	al. [9]	0					g	CRL=0.7	30  mg	
		1						2 cm		
		8						RT		
								interstitia		
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0					froze		omatic	IUP –	n +	
					n embr			CRI 11	local MTX	
					yos			cm for	20 mg	
								LT	LT	
								interstitia	cornua	
q	Wan		29	FUD	2	7147+1	Worson	I – 4 Cm Viable	I Lanaro	30117
	g et	202	25	LUI	froze	d	ing pain	IUP	scopic	uncomp
	al. [10]				n embr		in the lower	LT	Cornua	licated CS
	[10]				yos		LT .	interstitia	1	
10	-		27	FUD	2	0	abdomi	l – viable	resecti	Birthwe
10			52	EUP	fresh	9w+3 d	inal	IUP	scopic	re CS at
					embr		pain	IT		34w (fotal
					yus		_	interstitia	l	distress)
11			30	EUP	2   fresh	7w	Asympt	Viable IUP	Laparo scopic	Full- term CS
					embr		omatic	101	LT	
					yos			interstitia	l l	
12	Ben-	200	35 With	EUP,	3	7w	Crampi	RT	Laparo	Uncom
	et al.		recu		Day		lower	pregnanc	resecti	term
	[11]		rrent HP		3   embr		abdomi	y (2 cm	on of	singleto
			1.11		yos				stump	vaginal
13	Shav	201	35	Hydros	2	6w		Rt stump	Laparo	Missed
	al.	5			Day			y y	resecti	8w
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14			35	Hydros	2	6w		LT stump	Laparo	Missed
				alpinx				pregnanc v	scopy -	abortion
								5	on of	
					1		1			

EUP — ectopic pregnancy, LT — left, GS — gestational sac, IUP — intrauterine pregnancy, US — ultrasound, CS — cesarean section, KCL — potassium chloride, PRBCs — packed red blood cells, MC-DA — monochorionic-diamniotic, HP — heterotopic pregnancy, PID — pelvic inflammatory disease, RT — right, CRL — crown rump length, MTX — methotrexate

Figure 3. Flowchart of the articles and the patients included in the review.

.Figure 3

(Records identified through the search (n = 15

(Excluded (n = 6 -

Articles not reporting heterotopic interstitial/tubal stump plus intrauterine pregnancies (n = -

(3

Articles not reporting cases after bilateral salpingectomy -

(Articles includet in the review (n = 9

(Patients included in the review (n = 13

Figure 3.



#### DISCUSSION

HP is an extremely rare event in the general population, but occurs more frequently in women who undergo IVF, in which more than one embryo may be transferred. After bilateral total salpingectomy EUP are still possible; and interstitial, cornual, cervical, broad ligament, ovarian, and primary abdominal pregnancies have been reported [13, 14]. The exact mechanism behind HP subsequent to bilateral salpingectomy remains uncertain. Potential causative risk factors include the presence of the residual interstitial portion of the fallopian tube and the formation of a cornual sinus post-laparoscopic salpingectomy. Consequently, it is crucial to conduct laparoscopic sterilization meticulously to minimize tubal residue [10]. The patient described in this case report underwent bilateral salpingectomy at another institution, and although she reported no complications from the procedure, we lack specific data regarding it. Furthermore, she did not undergo hysterosalpingography or hysteroscopy following this surgery. Therefore, the theoretical possibility of small iatrogenic canals connecting the uterine cavity to the abdomen cannot be ruled out.

Risk factors for EUP in an IVF cycle include pelvic inflammatory disease, previous EUP, endometriosis, and smoking [15]. Furthermore, IVF is associated with an increased risk of HP due to multiple embryo transfer [16]. Forty-six percent (6 of 13) of the women included in our review had only two embryos transferred, but all of them had a history of EUP or tubal infertility. In one woman, three embryos were transferred [6], but an interstitial pregnancy of monochorionic-diamniotic twins was diagnosed, together with intrauterine twin pregnancy. A dose-response relationship between the risk of ectopic pregnancy and the number of embryos transferred during an ART cycle has been reported [17]. This is likely due to advancements in IVF techniques leading to enhanced implantation potential and increased likelihood of extrauterine implantation. Despite the increased utilization of ultrasound guidance during embryo transfer procedures since the late 1990s, a meta-analysis revealed no reduction in ectopic pregnancy rates associated with its implementation [18].Notably, spontaneous EUP after bilateral tubal salpingectomy or tubal ligation might also occur [19].Most of the women reported here presented at 6–7 weeks of pregnancy; the

diagnosis was delayed in one, although she already complained of abdominal pain at 12w of her pregnancy. She was eventually diagnosed with a ruptured interstitial pregnancy at 26w and underwent emergent laparotomy; two viable fetuses were delivered and survived [6]. This illustrates that a diagnosis of interstitial pregnancy might be challenging especially if it is a part of HP, which can falsely reassure the examiner.

Interstitial pregnancies are commonly believed to be associated with delayed ruptures compared with other tubal pregnancies because the myometrium is more distensible than the fallopian tube. However, a recent review demonstrated that most interstitial pregnancies are diagnosed in the first trimester [20]. Early diagnosis is fundamental to managing this condition safely and is accomplished using antenatal US. US diagnosis of interstitial pregnancy is based on the following criteria: location of the GS outside the uterine cavity; adjoining of the interstitial part of the fallopian tube with the lateral aspect of the uterine cavity and the GS; and extension of the myometrial mantle laterally to encircle the GS [21].

Although most of the women included in this review had vaginal bleeding and/or abdominal pain, two had no symptoms at diagnosis and one of them had a 4 cm mass of left interstitial pregnancy [11, 12]. A previous report showed that almost half of interstitial pregnancies were diagnosed during routine scans in asymptomatic women [20]. The classic triad of EUP-abdominal pain, amenorrhea, and vaginal bleeding occurs in less than 40% of women with interstitial pregnancy [22]. Of the three women with tubal stump pregnancies, we found data on only one; she presented at 7w with abdominal pain and was hemodynamically unstable.

The treatment choice of heterotopic pregnancy must consider synchronous intrauterine pregnancy, which can be viable and desirable. Furthermore, treatment should be determined by gestational age at presentation, symptoms, US findings, and the viability of the interstitial pregnancy. Medical treatment includes local injection of KCL, hyperosmolar glucose, methotrexate (MTX), or hypertonic NaCl. Only two of the women in this review were medically treated with local KCL and MTX [4, 9]. Furthermore, successful treatment consisting only of aspiration has been reported. Women who do not undergo surgical treatment should be followed carefully, as rupture might still occur. Our patient was initially treated by aspiration but eventually underwent an emergent laparoscopic cornual resection due to rupture.

Forty-two percent (5 of 11 women with interstitial HP included in our review) had rupture and 83% of the included women underwent surgical treatment. Thus, operative management remains a mainstay as it offers a definitive diagnosis and treatment. Surgical treatment of interstitial pregnancy is done by laparoscopy or laparotomy and consists of cornual resection or cornuostomy. Hemodynamically unstable patients might eventually undergo hysterectomy [23]. While cornual resection carries an increased risk of uterine rupture due to the loss of myometrium and extensive uterine scarring, cornuostomy removes the interstitial pregnancy, while preserving the uterine myometrium and reducing the risk of uterine rupture [23]. All the women with heterotopic tubal stump pregnancy in this review had a laparoscopic resection. Pregnancies located in the tubal stump are also prone to rupture and excessive blood loss due to the rich blood vasculature from branches of both the ovarian and uterine arteries in that area.

Most patients included in this review underwent an uneventful elective cesarean section due to the increased risk of uterine rupture following cornual resection. One woman with a tubal stump pregnancy (who underwent cornual resection) had an uncomplicated term vaginal delivery. Whether laparotomy or laparoscopic surgery is performed, the perioperative period has a good prognosis, and the fetus can be delivered in the last trimester.

In conclusion, after bilateral total salpingectomy women are still at risk of HP. This risk may be reduced by the reduction in the number of transferred embryos in IVF. HP is a challenging condition to diagnose and treat. For those who wish to preserve the intrauterine pregnancy, cornual resection can be performed with good prognosis.

#### Article information and declarations

#### Data availability statement

Data regarding the subject of the case report has not been previously published. Data will be made available to the editors of the journal for review or query upon request.

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#### **Conflict of interest**

The authors have nothing to disclose.

### Supplementary material

None.

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