

# Tubal Stump Pregnancy in ART Patients

## Two cases of ectopic stump pregnancy after IVF-ET



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### Abstract

Ectopic pregnancy (EP) is a complication of pregnancy in which the embryo attaches outside the uterus. The rate of ectopic pregnancy is about 1 and 2% that of live births, though it may be as high as 4% among those using assisted reproductive technology (ART). We present two cases of interstitial stump pregnancies in patients who previously underwent salpingectomy for ectopic pregnancies, and a review of the literature. One patient has been treated with methotrexate (MTX) before the removal of the tubal stump, while the second has gone directly to laparoscopic (LPS) surgery. Transvaginal ultrasound examination is essential for early and accurate management of this condition. It should be quickly performed to rule out a stump interstitial pregnancy in women who conceive by ART after bilateral salpingectomy. A correct attitude towards this condition is not yet internationally standardized and both medical and surgical options should be promptly considered.

**Keywords:** Ectopic pregnancy (EP); Assisted reproductive technologies (ART); Tubal stump; Methotrexate (MTX); *In vitro* fertilization (IVF)

**Abbreviations:** EP: Ectopic Pregnancy; ART: Assisted Reproductive Technologies; MTX: Tubal Stump Methotrexate; IVF: *In Vitro* Fertilization

### Introduction

Ectopic pregnancies (EP) represent the most serious complication of the first trimester of pregnancy. In the vast majority of the cases the embryo prematurely implants itself in the fallopian tube before arriving in the uterine cavity. Only in approximately 2% of the cases EP occur in different regions such as the cervix, the ovary or the abdominal cavity [1-5]. An atypical and insidious severe event is that the embryo migrates from the uterine cavity

to the contralateral tube. We report two cases in which the EP occurred in a fallopian stump after *in vitro* fertilization (IVF) in women subjected to monolateral salpingectomy for a history of ectopic pregnancy. We present also a review of literature about interstitial pregnancies in tubal stump (Table 1) and a review about EP in unusual sites in women with previous salpingectomy (Table 2) [6-10].

**Table 1:** Review of literature: interstitial pregnancies in tubal stump.

Author	Year	Age	Gravity and parity	Previous operation history	Mode of conception	Gestation, weeks	Management	Internal Bleeding
Corti,Rolandi [1]	1964	35	G3,P2	Appendectomy, left salpingo-oophorectomy for a serous ovarian cyst	Spontaneous	5+3d	Subtotal hysterectomy	50 ml
Benzi [2]	1967	27	G2,P0	Righ salpingo- oophorectomy for ectopic pregnancy	Spontaneous	5	Laparotomic excision of right tubal stump	Poor
Krzaniak [3]	1968	30	G2,P2	Appendectomy, Ovarian cystectomy	Spontaneous	9	Laparotomic excision of left tubal stump	None
Bernardini [4]	1998	36	G4,P0	Appendectomy, Left salpingo-oophorectomy for interstitial tubal pregnancy	Spontaneous	4+5d	A single i.m. dose of MTX (100 mg) on day 61 of gestation	NA

Takeda [5]	2006	36	G1,P1	Laparotomic right salpingo-oophorectomy for an ovarian dermoid cyst	Spontaneous	8	Laparoscopic excision of right tubal stump	20 ml
		27	G3,P2	Laparoscopic right salpingo-oophorectomy for ruptured ovarian pregnancy	Spontaneous	6	Laparoscopic excision of right tubal stump	100 ml
Milingos [6]	2008	38	G6,P3	Laparoscopic right salpingectomy and laparoscopic excision of the right tubal stump	Spontaneous	5+6d	Laparotomic excision of right tubal stump and left salpingectomy	NA
Faleyimu [7]	2008	22	G2,P0	Left corneal resection for tubal pregnancy	Spontaneous	5	Laparotomic left salpingo-oophorectomy	600 ml
Muppala [8]	2009	38	G3,P1	Right salpingectomy for tubal pregnancy	Spontaneous	6	Laparoscopic cauterisation of right bleeding tubal stump	500 ml
Sturlese [9]	2009	30	G1,P0	Left salpingo- oophorectomy for an ovarian dermoid cyst	Spontaneous	6	Laparoscopic excision of left tubal stump	NA
Ko PC [10]	2011	30	G2,P0	Laparoscopic right salpingectomy for tubal pregnancy	Ovulation induction	8	Laparoscopic excision of right tubal stump	500 ml
		40	G7,P4	Laparoscopic right salpingectomy for tubal pregnancy	Ovulation induction	6	Laparoscopic excision of right tubal stump	550ml
		32	G4,P0	Laparoscopic left salpingectomy for tubal pregnancy	IVF-ET	8	Laparoscopic excision of left tubal stump	700ml
		30	G3,P0	Laparoscopic bilateral salpingectomy for right ovarian pregnancy and left tubal pregnancy after ICSI	ICSI-ET	7	Laparotomic excision of tubal stump	2000ml
		42	G3,P1	Laparoscopic left salpingectomy for tubal pregnancy after IUI	IVF-ET	7	Laparoscopic excision of left tubal stump	20ml
		32	G4,P0	Laparoscopic bilateral salpingectomy for bilateral hydrosalpinx	ICSI-ET	6	Laparoscopic excision of tubal stump	200ml
Garavaglia [35]	2012	33	G4 P0	partial left salpingectomy and right total laparoscopic salpingectomy	IVF-ET	3	Laparoscopic resection of the left tubal stump	100ml
		37		bilateral laparoscopic salpingectomy for bilateral hydrosalpinx	IVF-ET	4	laparoscopic right cornuostomy.	NA
Shavit T. [36]	2013	35	G0 P0	laparoscopic bilateral salpingectomy due to hydrosalpinges	IVF-ET	2	Laparoscopic excision of tubal stump	NA
Bahareh Samiei- Sarir [37]	2013	42	G11 P7	Laparoscopic right salpingectomy for tubal pregnancy	Spontaneous		monopolar/bipolar diathermy plus tubal ligation on the left side.	500 ml
		35	G8 P2	Laparoscopic left salpingectomy for tubal pregnancy	spontaneous	7	Laparoscopic excision of left tubal stump	2000 ml
Maruthini et al [38]	2013	33	G0P0	bilateral laparoscopic salpingectomy for bilateral hydrosalpinx	IVF-ET	6	Laparoscopic then Laparotomic excision of tubal stump	300ml
Nishida M [39]	2015	26	G4 P1	Laparoscopic right salpingectomy for tubal pregnancy	spontaneous	6	Laparoscopic excision of left tubal stump, removal of the gestational sac	NA

Xu Ying et al. [40]	2016	28	G0	bilateral tubal ligation for left hydrosalpinx and right tubal occlusion	IVF-ET	7	Emergency LPTM for left ruptured interstitial pregnancy	500 ml
Souza C. [41]	2018	35	G3 P1	Laparoscopic right salpingectomy for tubal pregnancy	IVF-ET	NA	Right salpingectomy	NA

**Table 2:** Review of literature: EP in unusual sites in women with previous salpingectomies.

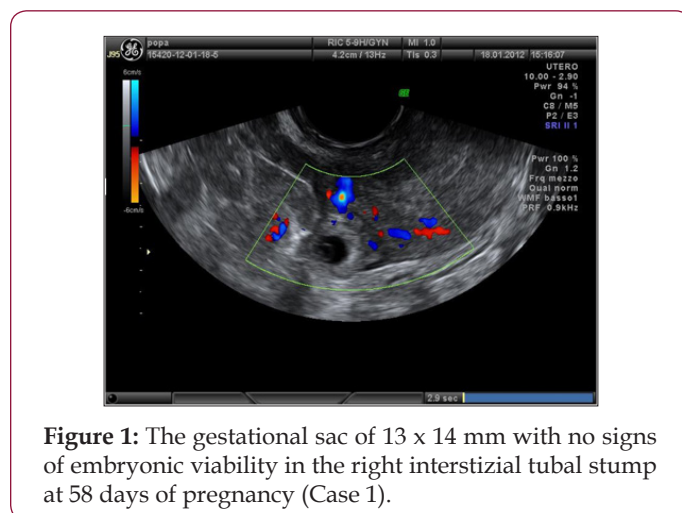
Author	Year	Age	Gravity and parity	Previous operation history	Type of fecondation	Site of ectopic pregnancy	Management
Ferland [11]	1991	32	G4,P0	right salpingectomy for tubal pregnancy	IVF-ET	upper retroperitoneum	LPTM
Fisch [12]	1996	38	G2,P0	LPS (bilateral salpingectomy for two tubal pregnancies)	IVF-ET	abdomen (posterior aspect of the right broad ligament)	LPTM
Chen [13]	1998	28	G0	LPS (bilateral salpingectomy for hydrosalpinx)	IVF-ET	right uterine cornu	LPTM
		33	G1,P0	right salpingectomy for hydrosalpinx, right tuboplasty, successively left salpingectomy for tubal pregnancy)	IVF-ET	left uterine cornu	LPTM
		32	G0	bilateral tuboplasty for tubal disease	IVF-ET	right uterine cornu	LPTM
Dmowsky [14]	2002	34	G0	LPS (bilateral salpingectomy for hydrosalpinx)	IVF-ET	head of pancreas	LPTM
Cormio [15]	2003	30	G2,P0	LPS (bilateral salpingectomy for two tubal pregnancies)	IVF-ET	abdomen ( lower end of the omentum, adherent to the uterine fundus and cecum)	LPTM
Hsu [16]	2005	29	G0	LPS (bilateral salpingectomy for hydrosalpinx)	IVF-ET	ovary	MTX and LPS
Seshadri et al. [42]	2010	37	G0	Bilateral salpingectomies for two previous ectopic pregnancies in 2001 and 2004	IVF-ET	ovary	LPS then converted to LPTM
Cruciani [17]	2011	26	G0	LPS (bilateral salpingectomy for hydrosalpinx)	IVF-ET	ovary	LPS
Sadia Khandaker et al. [43]	2015	32	G5P1	Right (2007) and left (2009) salpingectomy for tubal pregnancies	IVF-ET	ovary	LPS then converted to LPTM
Xu Ying, et al. [39]	2016	28	G3P0	right LPS salpingectomy after two tubal pregnancies+ left bipolar salpingectomy for hydrosalpinx	IVF-ET	ovary	Emergency LPTM

**Case report**

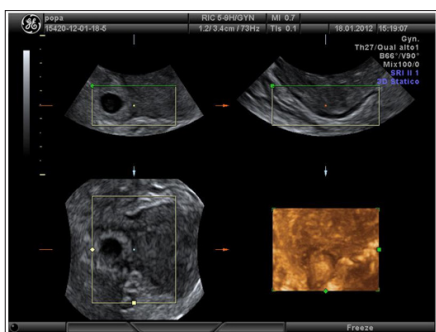
**Case 1**

A 36 years old patient referred to our center to ascertain implantation after IVF-ET at the 58<sup>th</sup> gestational day. The patient had a history of right salpingectomy for GEU. HCG was 2293 IU/L. Obstetrical examination showed a small uterus with no pain. Ultrasound revealed no intrauterine pregnancy, but a gestational sac of 14 mm adjacent to the right uterine cornu with no signs of embryo viability. Power and color Doppler revealed the presence of the vascular ring with a strong peri-trophoblastic vascular activity (Figures 1 & 3). After careful counseling it was decided to attempt medical management using the single dose regimen with i.m. MTX (50mg/m<sup>2</sup>). Four days after treatment the patient complained strong abdominal pains, low blood pressure and severe anemia. Laparoscopy was carried out and the right tubal stump was removed. Histological examination confirmed the diagnosis of ectopic pregnancy of the right tubal stump. The patient was

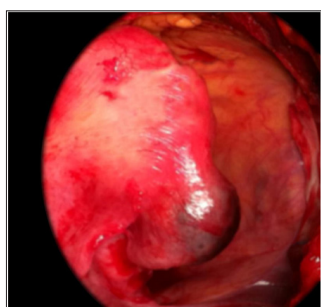
discharged on day 2 postoperatively and no short- or long-term complications were reported [11-17].



**Figure 1:** The gestational sac of 13 x 14 mm with no signs of embryonic viability in the right interstitial tubal stump at 58 days of pregnancy (Case 1).



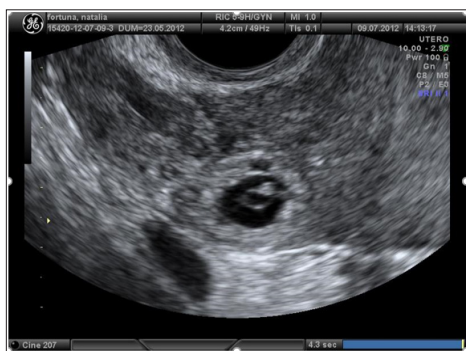
**Figure 2:** 3D reconstruction of interstitial tubal stump pregnancy (Case 1).



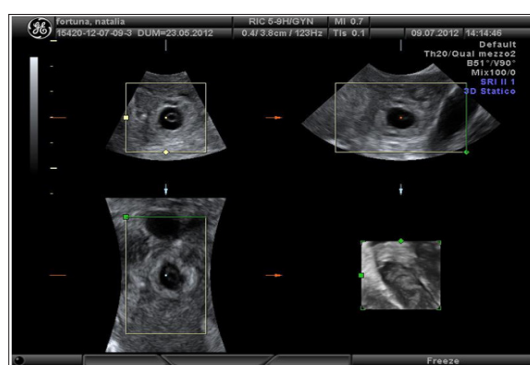
**Figure 3:** The right tubal stump with the ectopic pregnancy of about 20 mm in diameter (Case 1).

### Case 2

A 25 years old patient referred to our emergency Department for pain in the right iliac fossa. She was at 7 weeks of gestation after embryo transfer achieved by ICSI. The patient had a history of right salpingectomy for GEU. Pelvic examination revealed pain in the right adnexal area and US showed a gestational sac of 11 x 10 mm with no signs of embryonic viability in the right interstitial tubal stump (Figures 4 & 5) and hemoperitoneum. HCG was 8839 IU/L. The patient was subjected to an emergency laparoscopy and the right tubal stump was removed. Histological examination confirmed the diagnosis of ectopic pregnancy in the right tubal stump. The patient was discharged on day 2 postoperatively and no short- or long-term complications were reported.



**Figure 4:** The gestational sac of 11 x 10 mm with no signs of embryonic viability in the right interstitial tubal stump pregnancy (Case 2).



**Figure 5:** 3D reconstruction of interstitial tubal stump pregnancy (Case 2).

### Discussion

Though the etiology of EP is multifactorial, as many as 50% of women with an EP have no identifiable risks. Widely accepted risks for EP are not necessarily independent of one another and can vary depending on the population being reported. Risk factors include prior EP, prior tubal and generally pelvic surgery, IUD and a history of pelvic inflammatory disease (PID) [18]. In patients undergoing ART, the chances of an embryo spontaneously implanting at the interstitial tubal segment are higher when compared to a spontaneous pregnancy [19]. Tubal stump pregnancies can occur when the embryo or the oocyte migrate through the uterine cavity or when the oocyte passes through a tubal fistula [3,9]. A review of the literature conducted by Chin et al. [20] reported 22 cases of cornual pregnancies after IVF-ET.

In women with a history of salpingectomy, some cases of unusual implantation sites have been reported. Fisch et al. [12] in 1996 reported a case of an abdominal pregnancy following in vitro fertilization in a woman subjected to bilateral salpingectomy. Dmowsky et al. [14] reported a retroperitoneal ectopic pregnancy located in the head of pancreas in a similar patient. Ferland et al. [11] reported a retroperitoneal pregnancy in a patient with previous right salpingectomy secondary to an ectopic gestation. Agarwal et al. [21] studied 26 ectopic pregnancies detected after embryo-transfer during a 7-year period and seven were located in the cornual or tubal stump after prior salpingectomy. Four out of seven women were treated with MTX, but in only one case conservative treatment was successful. The other three cases were tubal implantations, with one rupture during treatment. Chang et al. [22] presented a case of bilateral simultaneous tubal sextuplets pregnancy after in-vitro fertilization-embryo transfer following salpingectomy. Chen et al. [13] described three cases of cornual pregnancies occurring after IVF-ET.

Two of these patients had prior bilateral salpingectomy, whereas another had prior tuboplasty for tubal disease. Nabeshima et al. [23] presented the case of a 38-year-old woman, with a history of left salpingectomy for an ectopic pregnancy, admitted for treatment of another presumed ectopic pregnancy. Surgery was performed for a suspected left cornual pregnancy and with

laparoscopy the gestational sac was removed; the uterus was preserved. Unilateral and even bilateral salpingectomy cannot prevent subsequent heterotopic pregnancy. Even more catastrophic conditions may occur because the ectopic gestation is always located within the interstitial tubal portion, rather than in the ampullary portion of the fallopian tube [24]. The uterine cornu has an abundant blood supply from branches of the ovarian and uterine arteries and a ruptured cornu can have tragic consequences from sudden and excessive blood loss. For this reason, these pregnancies are generally associated with very high serum HCG levels and the mortality rates for interstitial pregnancy are estimated to be 7-15 times higher than another EP [25].

At the beginning, the traditional treatment for interstitial pregnancy was cornual resection by laparotomy or hysterectomy [26]. In the last decades operative laparoscopy has generally been considered the "gold standard" for the treatment of tubal ectopic pregnancies [27], but medical treatment is viewed with increasing interest. The medical treatment is of particular relevance in the case of infertile patients for whom any avoidance of additional surgical intervention translates into a reduced risk of repeating ectopic pregnancy, in addition to maximal preservation of their future fertility potential. The estimated success rate for medical treatment with methotrexate of interstitial pregnancy is lower than that for treatment of ectopic pregnancies located in the tubal ampulla or isthmus [28]. Although medical therapy can be successful at serum HCG concentrations considerably higher than 3000 IU/l, quality-of-life data suggest that methotrexate is only an attractive option for women with an hCG below 3000 IU/l [29-31].

In 2016, the Royal College of Obstetricians and Gynaecologists (RCOG) released a new guideline providing evidence-based guidance on the diagnosis and management of ectopic pregnancies [32]. Concerning interstitial or cornual pregnancies, it pointed out that even if a pharmacological approach using methotrexate has been shown to be effective, there is insufficient evidence to recommend local or systemic approach. Moreover, RCOG guideline has confirmed the main role of surgery in the management of cornual pregnancy with conservative, laparoscopic or open surgical methods, and it reported medical therapy with methotrexate and potassium chloride injection as an option prior to later laparoscopic horn excision. Nevertheless, an international consensus on the management of cornual or stump pregnancy is still far, as all the evidence reported in the guideline come from non-analytical studies, such as case reports or are based on expert opinion.

Reviewing the literature, we found only one case of tubal stump pregnancy treated successfully with a single i.m. dose of MTX (100 mg) with a serum HCG concentration of 12.470 IU/ml [4]. The presence of cardiac activity in an ectopic pregnancy is associated with a reduced chance of success following medical therapy and should be considered a contraindication to medical treatment [32,33]. Therefore, a similar behavior should be considered for EP of the tubal stump. In conclusion, early transvaginal ultrasound should be considered in women with a history of salpingectomy in

order to allow early diagnosis of EP of the tubal stump. Physicians should remember to consider this severe condition when surgically treating conditions such as PID and EP and remove the fallopian tube entirely [34-43].

### Disclosure Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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