Rare uterine serosal pregnancy after in vitro fertilization in a woman with bilateral salpingectomy

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Author contributions
Jun Tan and Ping-Ping Sun conceptualized the study. Shu-Yi Dong curated the data and conducted the formal analysis. The investigation was carried out by Shu-Yi Dong and Shu-Feng Liu. Shu-Yi Dong also handled the software. Jun Tan supervised the project. Validation was performed by Shu-Yi Dong, Shu-Feng Liu, Jun Tan, and Ping-Ping Sun. The original draft was written by Shu-Yi Dong, and the review and editing were done by Shu-Yi Dong, Shu-Feng Liu, Jun Tan, and Ping-Ping Sun.

Competing interests
The authors declare no conflicts of interest.

Abstract
Objective: To improve the understanding of ectopic pregnancy after bilateral salpingectomy through case analysis and literature review. Method: A case of uterine serosal pregnancy after in vitro fertilization and embryo transfer (IVF-ET) in a woman with bilateral salpingectomy was reported in detail and summarized, and relevant literatures searched in Pubmed were analyzed. Results: The patient had a sudden abdominal pain 18 days after transplantation. Ultrasound showed no pregnancy sac in the intrauterine cavity and bilateral adnexal areas, but there was a large amount of fluid in the Pouch of Douglas, which was an indication for surgical exploration. During the operation, the pregnancy tissue was found on the uterine serosa and cleared in time. And the patient recovered well after surgery. Review of the literatures showed that most of ectopic pregnancies after bilateral salpingectomy were treated surgically and had a good prognosis. Conclusion: Ectopic pregnancy after bilateral salpingectomy is extremely rare and should be early judged by the patients/signs. Surgical treatment timely can achieve good outcome.

Keywords: IVF-ET; uterine serosal pregnancy; ectopic pregnancy; bilateral salpingectomy
**Introduction**

Ectopic pregnancy (EP) rarely occurs after bilateral salpingectomy, but is still reported in clinical practice, especially the widespread use of In Vitro Fertilization and Embryo Transfer (IVF-ET) for infertile couples worldwide [1, 2]. Interstitial pregnancy is the most common, and pregnancy in other parts, such as abdominal pregnancy [3], ovarian pregnancy [4], cervical pregnancy [5], are occasionally reported. But some rare EP or even usually considered impossible EP in a natural pregnancy may occur after ART, such as the case presented here. This is a rare type of EP, uterine serosal pregnancy, which is a very low incidence in the clinic and easy to miss diagnosis and misdiagnosis. This paper reviewed the clinical data of this rare case of uterine serosal pregnancy after IVF-ET with bilateral salpingectomy as well as summarized the relevant literature reports, which provided a reference for the diagnosis and management of patients with abdominal pregnancy after bilateral salpingectomy.

**Case Report**

This case report was approved by the hospital's ethics committee (20231225001). The patient was a 37-years-old woman, gravida 3, para 1, ectopic pregnancies 2, known to have bilateral salpingectomy for EPs. She came to our reproductive center and required to adopt IVF to have a baby. So she had undergone IVF-ET in April 2023 because of tubal-factor infertility. One fresh embryo had been transferred and seven embryos had been frozen. The process of transplantation went very well. The patient's serum beta-human chorionic gonadotropin (β-hCG) level was 266.5 mIU/mL 14 days after ET. However, the patient had persistent dull pain in the lower abdomen after 18 days of ET, without vaginal bleeding and anal distension. At this time, serum β-hCG level was 1148 mIU/mL and transvaginal ultrasonography (TVUS) demonstrated no intrauterine gestational sac and an amount of fluid measured about 5.8 × 2.9 cm in the Pouch of Douglas, with no abnormalities in the bilateral adnexal region (Figure 1). Considering the persistent abdominal pain and unknown pregnancy, the patient was hospitalized for observation. But the patient had worsened abdominal pain after 22 days of ET. Again TVUS demonstrated there was still no intrauterine gestational sac but a mixed echo mass with a size of about 3.9 cm × 1.9 cm outside of the left ovary lateral, where no obvious blood flow signals were explored around (Figure 2). Gynecological bimanual examination revealed significant tenderness in the uterine body and the left adnexal area. Considering the possibility of intra-abdominal bleeding and not ruling out the potential of ruptured ectopic pregnancy, the patient underwent an urgent laparoscopic exploration. During the surgery, the uterus was observed to be enlarged as if at 40 days of gestation, with a regular shape. There was a purplish-blue discoloration on the serosa near the left fundus close to the uterine horn (Figure 3), which was approximately 0.5 cm. Below this area, a small rupture was visible with surface bleeding. Bilateral tubal absences and bilateral ovaries were grossly normal. There were blood clots in the uterine rectum pouch, and about 300 ml of dark red hematocoele in the pelvic cavity. After cutting open the purple-blue part of the uterus, the ectopic tissue was found to be superficial and did not reach the muscle layer. The abnormal tissue was removed and washed with saline, where a small amount of villus tissue was visible (Figure 4), MTX 50 mg was injected into the left uterine corner after surgery. The operation went well and the removed tissue was sent for pathological examination. Histopathology of the tissues confirmed the uterine serosal pregnancy, concordant with the intra-operative diagnosis (Figure 5). The patient recovered well after the operation and was discharged from the hospital three days later. The serum β-hCG dropped to normal two weeks after surgery.

![Figure 1 No intrauterine gestational sac with a amount of fluid measured about 5.8 x 2.9 cm in the Pouch of Douglas](https://www.tmrjournals.com/tcr)

![Figure 2 A mixed echo mass, approximately 3.9 cm × 1.9 cm, was observed outside the left ovary, with no significant blood flow signals detected around it](https://www.tmrjournals.com/tcr)
Figure 3 There was a purplish-blue discoloration on the serosa near the left fundus close to the uterine horn, approximately 1 cm × 1 cm in size.

Figure 4 There was a small amount of villus tissue in the removing abnormal tissue.

Figure 5 The histopathological examination showed villi tissue in the specimen removed from the uterine serosa (H&E, × 100).

**Literature review**

Uterine serosal pregnancy is considered to be a specific form of abdominal pregnancy, and the occurrence of abdominal pregnancy after bilateral salpingectomy has been reported few so far. A total of 92 articles (as of March 2024) were retrieved from the PubMed by entering the keywords “bilateral salpingectomy” and “abdominal pregnancy”. A total of 11 reports were selected by reading the abstracts or the full text, all of which were case reports (Supplementary Table S1).

**Discussion**

**Pathogenesis**

Uterine serosal pregnancy is an extremely rare ectopic pregnancy, which refers to the embryo swims outward and develops on the
surface of the uterine serosal membrane. The gestational sac is wrapped by the uterine serosal membrane, without obvious myometrial tissue, and is not connected to the fallopian tubes, endometrial cavity or round ligament [6]. This kind of the ectopic pregnancy is extremely rare, with only a few cases reported to date [7–9]. In fact, uterine serosal pregnancy is a special case of abdominal pregnancy. Theoretically, embryonic migration to abdominal implantation can be avoided after bilateral salpingectomy, but there were still some reports of abdominal pregnancy after bilateral salpingectomy in clinic, as shown in the Supplementary Table S1, all were case reports. The exact pathogenesis of the extrauterine implantation of embryos after bilateral salpingectomy is not clear, one may be related to IVF-ET [10, 11]. The difficulty of translantation or the volume of the injected culture medium, the depth of the transplant tube implantation in the uterine cavity, and the strength and speed of embryo injection may all affect the removal of embryos in the uterine cavity and increase the probability of ectopic pregnancy [4]. So IVF may be a predisposing for ectopic pregnancy in this patient. Alternatively, the embryo may be transferred to extrauterine via the subendometrial lymphatic circulation [3, 11], similar to bling the lymphatic metastatic pathway of endometrial carcinoma. The location of embryo implantation of in this case was in the uterine subsersa, where was not the uterine lymphatic circulation route. So it was considered that the lymphatic circulation route was not the main cause of morbidity in this patient. There was another possibility that this case was related to the formation of the tubal stump micro-fistula. It was reported that women underwent salpingectomy because of ectopic pregnancy, PID, or hydrosalpinx had a significantly increased risk of incomplete salpingectomy and subsequent microfistula compared with women underwent conventional salpingectomy [12, 13]. The embryo can enter the abdominal cavity through the fallopian tube stump fistula and implantation in the nearby tissue when the patient was pregnant again [13]. In this case, the implantation of the embryo was located on the uterine serosal surface near the left fallopian tube stump. It was speculated that the embryo may enter the abdominal cavity through the left tubal stump fistula, leading to the occurrence of this ectopic pregnancy.

Diagnosis
Uterine serosal pregnancy is easily missed or misdiagnosed because of lacking clinical manifestations’ peculiarity. Now the diagnosis of uterine serosal pregnancy mainly relies on serum β-HCG levels and transvaginal ultrasound. It reported that lower serum β-HCG levels 14 days after IVF-ET are associated with the possibility of ectopic pregnancy [14]. The serum β-HCG in this patient on 14 days after IVF-ET was 266.5 mIU/ml, which was lower and maybe a warning indicator for ectopic pregnancy. However, β-HCG levels are only proved to be pregnant and are difficult to estimate the location of gestational sac. TVUS is thought to be an important auxiliary examination in the diagnosis of location of gestational sac, which can assess the whole pelvis and discover ectopic lesions. The sensitivity of TVUS for the diagnosis of ectopic pregnancy mainly depend on the expertise of the ultrasonographer, the gestational age, and the type of ectopic pregnancy [9]. In this case, the reason for the lacking of gestational sac in TVUB was mainly related to the smaller gestational age and the rare implantation position of the embryo. In addition, the patient had a history of bilateral salpingectomy, which was easy to ignore the potential risk of ectopic pregnancy after pregnancy. Therefore, the diagnosis and treatment of the patient did not cause attention at the beginning, only just changes of the disease was observed. As the progression of the disease, the patient had aggravated abdominal pain, with a large volume of fluid in the Pouch of Douglas and a mixed echo mass outside of the left ovary lateral by TVUB. At this time intraperitoneal hemorrhage didn’t be ruled out and ectopic pregnancy was highly suspected. Therefore, emergency laparoscopic surgery was immediately performed and then uterine serosal pregnancy was found.

Conclusion
It is difficult to early diagnose because uterine serosal pregnancy is rare and lacks typical clinical symptoms. In general, pelvic hemorrhage has occurred when uterine serous pregnancy is found. Laparoscopic surgery is a mainly treatment method, which can not only make a clear diagnosis, but also assist in treatment. From this case, it can be seen that any pregnancy should be alert to the occurrence of ectopic pregnancy, regardless of whether the fallopian tube stump exists. The widespread use of IVF-ET make rare ectopic pregnancy become more common. Therefore, it is very necessary to be alert to ectopic pregnancy after IVF-ET, especially when TVUB cannot find the gestational sac. It should be give early diagnosis and treatment combining with the patients’ symptoms, signs and auxiliary examination to ensure the safety of the patients’ life.

References

