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Gene, Cell and Tissue
Article DOI: 10.5812/gct.114142
Published in: Gene, Cell and Tissue: In Press(In Press); e114142

# Peer Review Report for "Heterotopic Pregnancy After In Vitro Fertilization Ending with a Successful Term Labor, a Case Report"

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## Review Timeline:

Submit Date: 2 Mar 2021
Revised Date: 13 Mar 2021
Accepted Date: 15 Mar 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Reviewer | **Revision** (0) — 6 Mar 2021

Dear AE,
The paper appears comprehensive and the subject of the article is interesting. I have only a few concerns regarding the paper, please do check the grammatical mistakes, punctuation error, and verb or pronoun if they add incorrectly before the submission of the paper.
Thanks.

**REFEREE**: Reviewer | **Revision** (0) — 6 Mar 2021

Dear AE
The authors need to answer these comments
1- Write in vitro in italic form in all parts of the manuscript.
2- Please give reference to the introduction part.
Thanks.

**REFEREE**: Reviewer | **Revision** (0) — 7 Mar 2021

Dear AE,
Comments are expressed to improve the manuscript. Please refer to the attached file.

Thanks.

**Zahra Heidari**: Associate Editor | **Revision** (0) 8 Mar 2021

Dear EIC,
Based on the reviewers' comments and as I read, this manuscript needs major revisions and reply to the comment point by point.
Thanks.

**Zahra Heidari**: EIC | **Revision** (0) 8 Mar 2021

Dear Author,
Based on the reviewers' comments and as I read, this manuscript needs major revisions and reply to the comment point by point.
Thanks.

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Revision (1)

## Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Manuscript title: Heterotopic pregnancy after in vitro fertilization; A successfully treated case report.


## Abstract

Background: Heterotopic pregnancy is defined as the simultaneous presence of intrauterine and ectopic pregnancies manifested by abdominal pain and vaginal bleeding. Previous tubal surgeries and pelvic inflammatory diseases increases the risk of this anomaly. In this case study, a 32-year-old female with heterotopic pregnancy through IVF (*in vitro* fertilization) has been reported.

Case presentation: An 18-year-old female was referred to our medical department presented by abdominal pain and vaginal bleeding. She had IVF (*in vitro* fertilization) pregnancy 7 weeks ago and had no history of any other illness or drug history. According to ultrasound results, heterotopic pregnancy was diagnosed. Therefore, we decided to perform salpingectomy and laparotomy of the fetus and the patient had a normal delivery at term by cesarean section 38 weeks after pregnancy. The patient and her baby have been stable without any further refer for the mentioned condition.

Discussion: Due to the importance of heterotopic pregnancy and its prevalence among patients using fertility medications and assisted reproduction techniques such as IVF, even despite the observation of the gestational sac containing yolk sac and the embryo in the endometrium cavity, the adnexa should be well checked to rule out the heterotopic pregnancy diagnosis which can prevent the risk of abortion and such other fatal outcomes.


Keywords: Case Report, Heterotopic Pregnancy, *In Vitro* Fertilization

## Introduction

Heterotopic pregnancy is defined as the simultaneous presence of intrauterine and ectopic pregnancies manifested by abdominal pain and vaginal bleeding. Previous tubal surgeries and pelvic inflammatory diseases increases the risk of this anomaly.

Heterotopic pregnancy refers to the concurrent coexistence of an intrauterine and extrauterine pregnancy. In its early stages, the emergence of heterotopic pregnancy was nonspecific and accompanied by other abnormal manifestations of pregnancy (1). The prevalence of this event is very rare. However nowadays, it occurs with greater repetition and may lead a woman to life-threatening complications such as ruptured uterus and massive bleeding. Also, previous tubal surgeries and pelvic inflammatory diseases increases the risk of this anomaly (2). surgery could be a successful method to preserve most cases, if the intrauterine embryo survived and was diagnosed early. Careful investigation of the clinical or ultrasound adnexa findings in every asymptomatic patient is necessary and helpful for accurate diagnosis and sensible treatment plan (3).

We presented a case report of a heterotopic pregnancy who underwent *in vitro fertilization* (IVF) pregnancy in which salpingectomy and laparotomy of the fetus was performed in addition to ultrasound assessment, and had a normal delivery at term.

## Case presentation

A 32-year-old pregnant female presented to emergency room of our medical department with abdominal pain by spreading to feet and vaginal bleeding. She had IVF pregnancy 7 weeks ago and had no history of any other illness or drug history. Some of her vital signs were stable including: blood pressure 110/70 mmHg; and body temperature 38 ˚C; despite the pulse rate 125/bpm. The patient had a generalized abdominal tenderness and had no symptom of shortness of breath. Laboratory evaluation revealed that hemoglobin and hematocrit levels were 6%g and 19.1% respectively and lower than normal. Other biochemical results including white blood cell, blood urea nitrogen, mean corpuscular volume, creatinine and uric acid were within normal range.

Ultrasound results revealed intrauterine Gestational sac including yolk sac and fetal pole with normal heart activity in endometrial cavity. The yolk sac had normal size and shape. Estimated gestational age with crown lump length of 12 mm was 7 weeks and 3 days ± 4 days (Fig. 1). The trophoblastic tissue was seen circular. There was no subchorionic hematoma and internal os was closed. The ovaries were normal in size and shape. A 14*11mm isoechoic ringlike lesion was visualized in the left adnexa (Fig. 2). Color doppler also demonstrated the ring of fire sign (Fig. 3). Moreover a 40*22mm isoechoic irregular shape lesion was also visualized around it that was suggestive for clot (Fig. 4). Also, large amount of free fluid with internal echo was illustrated in the abdominal and pelvic cavities compatible with hemoperitoneum and suggestive for ruptured ectopic pregnancy (Fig. 5).

## Discussion

Heterotopic pregnancy is defined as the concurrent presence of intrauterine and ectopic pregnancies. Due to the increasing use of artificial reproductive techniques, the incidence of heterotopic pregnancies is increasing, but it still remains as an uncommon condition (4).

The prevalence of heterotopic pregnancy is estimated to be 1%-3% in women who have undergone the assisted reproduction technologies, especially ovulation induction pregnancy through IVF as in this case (5). The assisted reproduction technologies have increased the incidence of simultaneously existence intra- and extrauterine pregnancies, currently reported to be 9 in 10000 pregnancy (6).

Most site of the heterotopic pregnancies as in this patient, is the ampulla portion of the fallopian tube and is diagnosed when symptoms expand. The patients with previous tubal surgeries are at increased risk for the mentioned situation (7). The history of having an intrauterine device in patients with pelvic inflammatory disease increases the risk of having an ectopic pregnancy (8). This case was presented about 5 weeks after IVF with no remarkable past medical history.

Avoiding the life-threatening consequences of early diagnosis and treatment of heterotopic pregnancy such as hypovolemic shock, maternal mortality and fetal loss makes it a critical condition. However, due to possibility of intrauterine pregnancy existence, heterotopic pregnancy can be difficult to diagnose in its early stages. Accordingly, having prognostic heterotopic pregnancy risk factors makes the patient suspicious for the diagnosis. The amount of hemoglobin in our patient was remarkably below normal range in addition to the existence of free fluid containing internal echo in pelvis, presence of mass in adnexa and IVF history, which increased the suspicion for the heterotopic pregnancy diagnosis (9).

Heterotopic pregnancy is very uncommon in spontaneously occurring pregnancies and is associated with increased maternal and child mortality. According to this, careful investigation of

the clinical or ultrasound adnexa findings in every asymptomatic patient is necessary. Due to the importance of heterotopic pregnancy and its prevalence among patients using fertility medications and assisted reproduction techniques such as IVF, even despite the observation of the gestational sac containing yolk sac and the embryo in the endometrium cavity, the adnexa should be well checked to rule out the heterotopic pregnancy diagnosis. (3).

Finally, salpingectomy and laparotomy of the fetus was performed and the patient had a normal delivery at term by cesarean section 38 weeks after pregnancy. As far as follow-up, the patient and her baby have been stable without any further refer for the mentioned condition.

## Conclusion

Considering the importance of heterotopic pregnancy and its high-rate occurrence among patients using assisted reproduction techniques such as IVF, even despite the observation of the gestational sac containing yolk sac and the embryo in the endometrium cavity, the clinicians should pay special attention checking the adnexa to rule out the heterotopic pregnancy diagnosis.

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**Revision (1)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Reviewer | **Revision** (1) 14 Mar 2021

Dear AE,
The author has made corrections.
Thanks.

**REFEREE**: Reviewer | **Revision** (1) 14 Mar 2021

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

**REFEREE**: Reviewer | **Revision** (1) 15 Mar 2021

Dear AE,
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Thanks.

**Zahra Heidari**: Associate Editor | **Revision** (1) 15 Mar 2021

Dear EIC,
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Thanks.

**Zahra Heidari**: EIC | **Revision** (1) 15 Mar 2021

Dear Authors,
Based on the reviewer's and AE's comments, revisions were done well. Thus this manuscript can be accepted for publication in GCT.
Thanks.