

Heterotopic pregnancy with superfetation following ovarian stimulation: A case report

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ARTICLE INFO

Keywords:

Assisted reproductive technologies
Case report
Clomiphene citrate
Ectopic pregnancy
Heterotopic pregnancy
Ovarian stimulation
PID
Salpingectomy

ABSTRACT

Heterotopic pregnancy (HP) is a rare phenomenon. Despite its rarity, there has been a notable increase in its incidence in recent decades due to the greater use of in vitro fertilization (IVF). However, information about the relation between ovarian stimulation and HP is scarce. We report a case of HP after ovarian stimulation using clomiphene citrate.

A 26-year-old pregnant woman presented to the emergency department with mild vaginal bleeding, and abdominal pain. She had a history of pelvic inflammatory disease (PID) and left salpingectomy due to a previous ectopic pregnancy. She had undergone ovarian stimulation with clomiphene citrate three months earlier. Transvaginal ultrasound revealed an eight-week-old ruptured tubal pregnancy with an intrauterine ten-week-old gestational sac confirming superfetation HP. An urgent laparoscopic right salpingectomy was performed and the extrauterine pregnancy was successfully removed with the preservation of the intrauterine embryo. The course of the intrauterine pregnancy was uneventful and the patient gave birth to a healthy boy via cesarean section.

Women receiving ovarian stimulation are at an increased risk of developing HP especially when they also have other predisposing factors for HP. Thus, close monitoring using transvaginal ultrasound with extra attention to the adnexa is required for a timely diagnosis and management of HP.

1. Introduction

Heterotopic pregnancy (HP) is a rare phenomenon in which intra- and extra-uterine pregnancies coexist [1]. The same factors that predispose to ectopic pregnancy (EP) hold potential to cause HP. These include pelvic inflammatory disease (PID), previous EPs, previous surgeries involving the fallopian tubes, adhesions, the use of assisted reproductive technologies (ARTs), such as in vitro fertilization (IVF) and intrauterine insemination (IUI), and ovarian hyperstimulation syndrome (OHSS) [2–4].

The overall incidence rate of HP is low. However, it has increased over the years. It reached 1% of all patients undergoing IVF in the 1990s [4]. This is due to increased number of embryos transferred when using ARTs, especially in women with previous tubal or pelvic disease, and the use of transvaginal ultrasound (TVUS) for diagnosis [4].

Ovarian stimulation is one of the methods used to promote

conception in infertile women [5]. However, there is no clear information about ovarian stimulation as a risk factor for HP, with the literature consisting of cases only [6,7].

We report a case of induced tubal HP in a patient with a history of PID after receiving ovarian stimulation using clomiphene citrate (CC).

2. Case Presentation

A 26-year-old nulliparous woman presented to the emergency department at her tenth week of gestation complaining of mild vaginal bleeding. The bleeding started two hours before admission, with no history of trauma. She also complained of vomiting, appetite loss, abdominal pain, and fatigue. She had undergone a left salpingectomy seven months prior for an EP following a diagnosis of PID five months earlier. She underwent ovulation stimulation with CC 50 mg daily for ten days, three months prior to presentation. Upon admission, the

Abbreviations: ART, assisted reproductive technology; β -hCG, β -human chorionic gonadotropin; BMI, body mass index; CC, clomiphene citrate; CRL, crown-rump length; EP, ectopic pregnancy; HP, heterotopic pregnancy; IUI, intrauterine insemination; IVF, in vitro fertilization; MRI, magnetic resonance imaging; MTX, methotrexate; OHSS, ovarian hyperstimulation syndrome; PID, pelvic inflammatory disease; TVUS, transvaginal ultrasound.

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<https://doi.org/10.1016/j.crwh.2023.e00562>

Received 1 November 2023; Received in revised form 5 November 2023; Accepted 6 November 2023

Available online 7 November 2023

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patient was alert and oriented. Her body mass index (BMI) was 23 kg/m². Her vital signs were stable. The physical examination revealed right lower quadrant abdominal tenderness with no fever. The vaginal examination showed minimal bleeding with a closed internal os. Laboratory testing showed mild anemia and a white blood cell count up to $17.6 \times 10^3/\mu\text{L}$. The records for serum β -human chorionic gonadotropin (β -hCG) levels were unavailable. Other laboratory findings were within normal range.

Transvaginal ultrasonography (TVUS) revealed two gestational sacs with different gestational ages: an intrauterine sac with a crown-rump length (CRL) of 33 mm, equivalent to ten weeks of gestation, and a positive fetal heart pulsation appropriate for gestational age. The second gestational sac was in the right adnexa with a CRL of 22 mm, equivalent to eight weeks of gestation, with signs of rupture and a free fluid in the pouch of Douglas. These findings confirmed the diagnosis of superfetation HP. An urgent laparoscopy with right salpingectomy was performed to manage the ruptured extrauterine pregnancy (Fig. 1).

The extrauterine pregnancy was successfully removed with the tube; meanwhile, the intrauterine pregnancy was preserved. Close monitoring was applied with repeated TVUS showing normal embryo development. The pregnancy continued without any complication and the patient gave birth to a healthy boy at 38 weeks of gestation via cesarean section. Apgar scores were 7 and 9 at the first and fifth minutes after birth respectively.

3. Discussion

Heterotopic pregnancy is a rare condition with many risk factors [1]. Approximately 70% of women diagnosed with HP have at least one risk factor [8]. In the present case, the patient had three risk factors for HP: PID, the previous EP, and the pelvic operation. These put the patient at high risk for HP and EP.

Many indications for ovarian stimulation are known in infertile women [5]. However, the use of ovarian stimulation in fertile women depends on the situation. The present patient had suffered psychological stress from the loss of the previous pregnancy. Furthermore, the patient's husband was away from home for much of the time, with his employment. Therefore, the patient received ovarian stimulation, which is standard care for such cases in Syria.

The use of CC is associated with an increased rate of multiple pregnancies [9]. Furthermore, ovarian stimulation can lead to superfetation, although it is extremely rare [10]. However, information about the association between CC and HP is limited and mainly restricted to case reports [6,7]. As far as we know, there is no association between the dosage, and duration of CC in women suffering from HP after using CC [7,11]. However, the majority of these cases had no previous risk factors for HP [6,7]. This could suggest that ovarian stimulation can be a dependent risk factor for HP and emphasizes the importance of closely monitoring women who receive ovarian stimulation, especially when there are risk factors for EP and HP [3,12].

The diagnosis of HP may be challenging, as 50% of the cases in the first trimester are asymptomatic [13]. The β -hCG level is an unreliable indicator in HP patients [14]. TVUS plays a significant role in the diagnosis [15]. This technology is user dependent, as the examiner may get distracted by the finding of an intrauterine pregnancy thus omitting a complete examination of the adnexa [16]. Magnetic resonance imaging (MRI) can also aid the TVUS in diagnosing HP when the patient is stable and the TVUS is not definitive [17]. However, in the present case, the TVUS was enough to diagnose the HP.

The most common site of extrauterine pregnancy is in the fallopian tube [18]. Thus, late detection can lead to potentially life-threatening rupture of the extrauterine pregnancy [16], as in the present case. Early detection can aid in avoiding salpingectomy along with several other maternal complications [13].

The choice of treatment for heterotopic pregnancy depends on the situation [13]. Removal of the extrauterine pregnancy with laparotomy

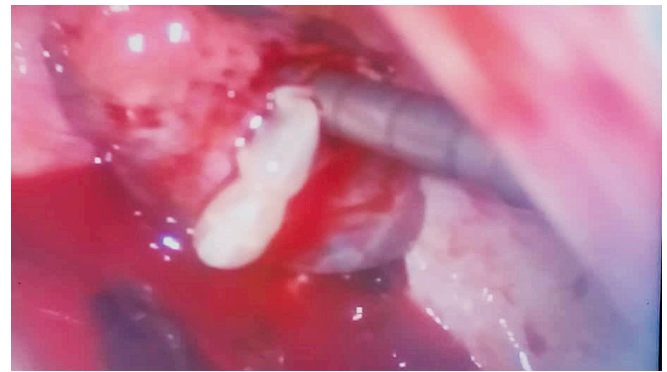


Fig. 1. Abdominal laparoscopic:
Legend: Right ruptured tubal ectopic pregnancy diagnosed through laparoscopy with blood in the peritoneal cavity.

or laparoscopy is the standard of care especially when it is in the fallopian tube [3]. However, a possible alternative treatment is the local injection of low-dose methotrexate (MTX) [19,20].

In conclusion, women receiving ovarian stimulation are at an increased risk of developing HP especially when they have other predisposing factors for HP. Thus, close monitoring using TVUS with extra attention to the adnexa is required for a timely diagnosis and management of HP. Furthermore, more studies with proper design are needed to clarify the indications of ovarian stimulation in patients with risk factors for HP and EP.

Contributors

Lilas Channiss contributed to drafting the manuscript and undertaking the literature review.

Tala Tahle contributed to drafting the manuscript and undertaking the literature review.

Rami Sabouni contributed to drafting the manuscript, undertaking the literature review and revising the article critically for important intellectual content.

Mohammed Jamalih contributed to patient care, conception of the case report, acquiring and interpreting the data, and supervised the work.

All authors have read and approved the final manuscript.

Funding

No funding from an external source supported the publication of this case report.

Patient consent

Written informed consent was obtained from the patient for publication of this case report.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Acknowledgements

The authors would like to thank Hadeel Mansour, Amjad Al Farraj, MD, Basma Khalil, MD, Reem Alatkee, MD, and Riad Cachecho, MD for their help and support.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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