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A case of heterotopic pregnancy after clomiphene-induced ovulation

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Abstract

Heterotopic pregnancy is a rare condition in which both intrauterine and extrauterine pregnancies occur simultaneously. It was reported to be very rare in normal conceived pregnancy. However, with the considerable progress of the assisted reproductive techniques, the incidence of heterotopic pregnancy increased. Furthermore, the incidence also increases in previous abortions. In this case report, we will present and discuss a patient who had heterotopic pregnancy after clomiphene-induced ovulation as well as a history of previous abortion where the extrauterine fallopian tube ruptured and was managed surgically while the intrauterine pregnancy was preserved.

Keywords

Case report, clomiphene, heterotopic pregnancy, ovulation

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Introduction

Heterotopic pregnancy is a rare condition in which both intrauterine and extrauterine pregnancies occur simultaneously.[1] The intrauterine fetus may be normal or dead with the intrauterine implantation occurring at the peritoneum, fallopian tube, uterine cornua, or cervix.[1] Heterotopic pregnancy usually happens when two or more ova are fertilized and implanted simultaneously intrauterine and extrauterine with an estimation rate of 1 out of 30,000 naturally conceived pregnancies.[2] However, assisted reproduction techniques are associated with significantly higher rate of heterotopic pregnancies reaching from 0.2% to 1% rate.[3] Furthermore, risk factors for heterotopic pregnancy include history of tubal surgery, ectopic pregnancy, pelvic inflammatory disease, and intrauterine device implantation.[1]

Case report

A 30-year-old lady gravida 2 para 0 (G2P0A1) presented to the emergency department at her seventh week of gestation complaining of mild left iliac pain associated with mild vaginal bleeding. Upon reviewing her history, both her medical and surgical histories were unremarkable except a history of a previous abortion at the seventh week in her first pregnancy. Meanwhile, her menstrual history showed regular occurrence cycles. The patient reported that this pregnancy was induced by clomiphene citrate due to a secondary infertility of 2 years after her last abortion.

On examination, the patient was vitally stable with a blood pressure reading of 120/75 mmHg, heart rate 90 beats per minute, and a temperature of 36.9°C. Upon abdominal examination, local tenderness at the lower abdomen was noticed particularly at the left iliac fossa. However, there was no guarding, rigidity, or palpable masses. Regarding vaginal examination, minimal bleeding was seen with a closed internal Ostium (OS).

Initially, her laboratory profile was unremarkable except for a mild leukocytosis of $16.3 \times 10^3/\mu L$ (normal range = 4000–11,000/μL), hemoglobin level was 12 g/dL (normal range = 12–16 g/dL), and platelets count of $307 \times 10^3/\mu L$ (normal range = 150–450). Her blood group was B+ while her bleeding profile showed an international normalized ration (INR) of 0.94, a partial thromboplastin time (PTT) of 11 s and an activated PTT of 28.8 s. Her beta human chorionic gonadotropin level (Beta-hCG) was more than 10,000 mIU/mL.

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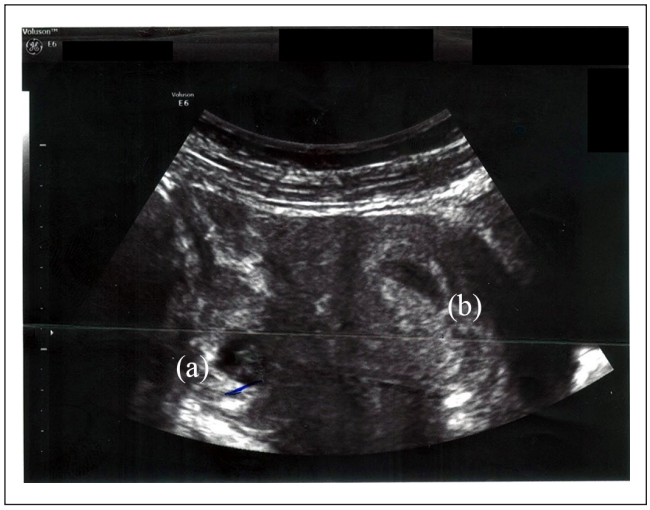

Figure 1. The patient's transvaginal ultrasound showing heterotopic pregnancy: (a) left ectopic pregnancy and (b) intrauterine pregnancy.

Transvaginal ultrasonographic examination revealed an intrauterine gestational sac with a crown-rump length (CRL) of 7 weeks and a positive fetal heart pulsation appropriate for gestational age. Meanwhile, another gestational sac was discovered and was identified as an ectopic pregnancy at the left iliac fossa with a CRL of 7 weeks and surprisingly a positive heart pulsation as well (Figure 1) along with moderate free fluid collection that was suspected to be blood in the Douglas pouch caused by the rupture of the ectopic gestational sac which was found to be in the left adnexa intraoperatively.

Results

A decision was made to treat the patient surgically and underwent an emergency laparotomy. Intraoperatively, a ruptured ectopic pregnancy in the left fallopian tube was found with moderate collection of blood in the Douglas pouch while the uterus was bulky and the right fallopian tube was normal. Moreover, left salpingectomy was successfully performed for the ectopic pregnancy without further operative complication. Postoperatively, the hemoglobin level dropped to 8.4 g/dL and two units of packed red blood cells (RBCs) were transfused. Transvaginal ultrasound was repeated and demonstrated normal intrauterine pregnancy with positive fetal heart pulsation. Furthermore, the histopathology report showed a disrupted oviduct wall with blood clots–entangled scattered chorionic villi covered by non-proliferated trophoblastic tissue. Finally, the pregnancy was uneventful afterwards with a vaginal delivery by the 40th week.

Discussion

Our patient presents a rare case of heterotopic pregnancy presenting in the typical gestational age of heterotopic pregnancy timeline, which ranges from the 5th and 12th weeks of gestation.[4] The patient was at a higher risk for heterotopic pregnancy than the general population due the use of clomiphene for induction of ovulation and her prior history of abortion. Induction of ovulation results was reported to be associated with a significantly increased risk for heterotopic pregnancy. According to Jeon et al.,[5] in their review of 48 cases of heterotopic pregnancy, ovarian hyperstimulation syndrome was the most potent risk factor. Patients with ovarian hyperstimulation syndrome had 10 times the tendency to develop heterotopic pregnancy than their counterparts from the general population (odds ratio (OR) = 10.7, $p = 0.009$).[5] The mechanism by which induction of ovulation causes heterotopic pregnancy is probably through increased probability of fertilization and consequent implantation of two or more stimulated ova.[2,6] This is why the incidence of heterotopic pregnancy increased significantly after the introduction of assisted reproduction techniques that are based on stimulation of ovulation.[5] Heterotopic pregnancy risk is also increased in cases with history of abortion. According to Jeon et al.,[5] patients with history of abortion were 3.9 times more prone to develop heterotopic pregnancy than normal healthy controls ($p = 0.003$). The mechanism by which abortion might be related to heterotopic pregnancy remains elusive. Theoretically, prior abortions might be a result of ectopic pregnancy that was missed.[7]

The most common clinical presentation in cases of heterotopic pregnancy is abdominal pain and tenderness. Around 80% of patients present with pain varying in site according to the location of extrauterine pregnancy in which vaginal pain occurs in about 15% of cases with palpable adnexal masses in about one half of patients.[5] While it is unlikely for both manifestations to occur concurrently, abdominal pain and vaginal bleeding was present in this case of heterotopic pregnancy which was confirmed by ultrasonography with vaginal sonography reported detection rate of 41%–84% of heterotopic pregnancies.[8] Meanwhile, the vaginal ultrasonography of this case found the extrauterine pregnancy in the fallopian tube which was reported to be the most common site of heterotopic pregnancy in the literature.[5,9] Heterotopic pregnancy might expose the patient and the fetus to various complications such as sac rupture leading to internal bleeding which may result in hypovolemia, in addition to pelvic inflammatory disease and adhesions may occur.[10,11] Regarding this patient's presentation, fallopian tube rupture was the cause of her abdominal pain and vaginal bleeding at the emergency department.

Management of heterotopic pregnancy remains controversial. The main aim of management is to remove the extrauterine pregnancy with the least invasive technique whether by ultrasound guided aspiration or surgically remove it to preserve the normal intrauterine pregnancy.[12,13] According to Majumder,[14] Beta-hCG serum assays along with vaginal ultrasound with adequate viewing of the adnexa is crucial in

detecting heterotopic pregnancies early in pregnancy. However, there is no well-established guideline on how to follow-up the intrauterine pregnancy after the removal of the extrauterine one whether surgically or by ultrasound–guided aspiration except to follow it as a regular pregnancy with close antenatal care until delivery.[15] Therefore, taking into consideration the capabilities of the facilities and the experienced practitioner, the guided aspiration according to the literature is regarded the least invasive way in removal of the extrauterine pregnancy. Meanwhile, laparoscopic removal is the preferred surgical approach, as it provides a minimally invasive approach as well with a lower propensity for blood loss, less postoperative pain, and fewer surgical wounds. In addition, it also provides a wide field for exploration in case the exact site was not well-visualized by the ultrasonography.[9,12] However, this case underwent laparotomic salpingectomy for the ruptured fallopian tube on the left side as a life-saving decision due to the internal bleeding without any complication occurring to the intrauterine pregnancy with good recovery outcome.

Conclusion

To conclude, ultrasound aspiration of the extrauterine sac is the preferred approach over surgery in hemodynamically stable patients while the laparoscopic approach for heterotopic pregnancy is the preferred surgical method of approach in hemodynamically unstable patients compared to a more invasive approach of laparotomy. However, as in our case, laparotomy was performed as a life-saving measurement after rupture of the extrauterine pregnancy.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical consideration

The patient provided us with the approval to use her case in making this case report as long as it does not provide any personal information.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article

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