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Ovarian pregnancy rupture following ovulation induction and intrauterine insemination: A case report

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Abstract

BACKGROUND

Ovarian pregnancy after assisted reproductive technology treatment has rarely been reported; ovarian pregnancy following intrauterine insemination (IUI) is even rarer, and only nine cases have previously been reported.

CASE SUMMARY

We report a case of ovarian pregnancy rupture after ovulation induction and IUI. The patient presented with bilateral lower abdominal pain and was referred to the emergency department. Ultrasound examination revealed ovarian pregnancy and intraperitoneal bleeding. Laparoscopy revealed an ovarian pregnancy with hemoperitoneum, which was subsequently removed. Pelvic adhesions were detected intraoperatively, which were treated immediately. The patient spontaneously conceived an intrauterine pregnancy 3 mo later, which was ongoing at the time of writing this study.

CONCLUSION

Close attention should be paid to any history of pelvic inflammatory disease before commencing IUI treatment, and patients with such a history should be closely followed up after IUI. Early measurement of serum β -human chorionic gonadotropin levels and ultrasonic examination are essential for timely diagnosis of ovarian pregnancy after ovulation induction and IUI to avoid more serious complications.

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Core Tip: Ovarian pregnancy following intrauterine insemination (IUI) is a rare complication with few case reports; ovarian enlargement due to ovulation induction increases the risk of ovarian rupture, causing severe bleeding. Close attention should be paid to patients with a history of pelvic inflammatory disease before commencing IUI treatment, and such patients should be closely followed up after IUI. Early measurement of serum β -human chorionic gonadotropin levels and ultrasonic examination could facilitate a timely diagnosis of ovarian pregnancy rupture after ovulation induction and IUI.

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INTRODUCTION

Ovarian pregnancy, a rare form of ectopic pregnancy (EP), constitutes approximately 0.5% to 3.0% of EPs, with a reported incidence ranging from 1 in 7000 to 1 in 40000 pregnancies[1,2].

The use of assisted reproductive technology (ART) is associated with a 0.15% to 1.00% incidence of EP[3]; nevertheless, ovarian pregnancy remains an extremely rare complication despite the increased incidence of EPs following assisted conception[1]. Herein, we present a case of ovarian pregnancy rupture following ovulation induction and intrauterine insemination (IUI), along with the relevant literature review. Further, we evaluate the current literature to understand ways to prevent and manage ovarian pregnancy following IUI.

CASE PRESENTATION

Chief complaints

The patient, a 28-year-old primigravida with a history of 43 d of amenorrhea, presented with bilateral lower abdominal pain and was referred to the emergency department. She reported having undergone IUI 30 d before presentation, owing to primary infertility for 3 years.

History of present illness

The patient had previously undergone ovulation induction and IUI twice. In the second IUI cycle, she underwent ovulation induction with letrozole 5 mg daily during days 5-9 of her menstrual cycle. Transvaginal ultrasound revealed one developed follicle in the right ovary, which was followed by the administration of 10000 IU of human chorionic gonadotropin (HCG) and IUI on the subsequent day. The initial serum β -HCG concentration was 130 mIU/mL 19 d after IUI, with a slower increase to 697.3 mIU/mL 26 d after IUI.

History of past illness

The patient had no history of sexually transmitted diseases, endometriosis, or previous gynecologic surgery. Nevertheless, the patient was positive for *Ureaplasma urealyticum* 3 mo before IUI but had no symptoms of urogenital tract infection. Hysterosalpingography revealed a normal uterus and bilateral patent fallopian tubes.

Personal and family history

The patient has a history of hyperthyroidism for 12 years. Through drug treatment, normal thyroid function was observed during IUI treatment. No family history.

Physical examination

The patient's body temperature was 36.3°C, heart rate was 78 bpm, respiratory rate was 20 breaths per minute, and blood pressure was 96/63 mmHg. Gynecologic examination in the emergency department revealed tenderness in bilateral adnexa uteri, with stable vital signs. About 5 mL of non-coagulated blood was obtained by puncturing the vaginal vault.

Laboratory examinations

The serum β -HCG level of the patient had elevated to 2817 mIU/mL 30 d after IUI.

Imaging examinations

Emergency transvaginal ultrasound examination revealed a uterus that was normal in size but without an intrauterine gestational sac, a 43 mm $\times$ 19 mm moderate echogenic mass located very close to the right ovary, and a 39 mm $\times$ 18 mm fluid dark area behind the uterus (Figure 1). A preliminary diagnosis of suspected ovarian pregnancy rupture (or rupture of corpus luteum) and hemoperitoneum was established. An emergency laparoscopy was planned. Intraoperative examination revealed a hemorrhagic mass surrounded by a blood clot on the surface of the right ovary. The mass was resected and subjected to pathologic examination. Histological examination revealed chorionic villi attached to the ovarian tissue (Figure 2).

FINAL DIAGNOSIS

The final diagnosis of the present case was ovarian pregnancy rupture after IUI.

TREATMENT

Emergency laparoscopic surgery revealed intraperitoneal hemorrhage amounting to 600 mL, with an approximately 1.5 cm $\times$ 1.0 cm $\times$ 1.0 cm hemorrhagic mass surrounded by a blood clot on the surface of the right ovary. Suspected chorionic villi were observed inside the mass, with a small rupture with evidence of active bleeding; the mass was resected and subjected to pathologic examination. Nevertheless, the right fallopian tube, contralateral ovary, and ovarian tube appeared normal. Notably, intraoperative examination revealed that the omentum was attached to the right pelvic peritoneum; meanwhile, the sigmoid colon was attached to the left pelvic wall. Pelvic adhesions were then treated.

OUTCOME AND FOLLOW-UP

The patient had a good postoperative recovery and was discharged on postoperative day 4. Follow-up examination revealed that her β -HCG level decreased gradually after the operation, reaching 2.05 mIU/mL on postoperative day 16. About 3 mo later, the patient spontaneously conceived an intrauterine pregnancy, which was still ongoing at the time of writing this study.

DISCUSSION

Although IUI is a widely used method of ART, it still carries a risk of EP. Ovarian pregnancy is an extremely rare complication after IUI; it may cause pelvic bleeding or ovariectomy, and even circulatory collapse, which could be life threatening[4].

Spiegelberg[5] reported that for an EP to be classified as ovarian pregnancy, the fallopian tube and its fimbriae should be intact and separate from the ovary, the normal position of the ovary should be occupied by the gestational sac, the ovary and the uterus must be connected by the utero-ovarian ligament, and the ovarian tissue must be present in the wall of the gestational sac. All these criteria were fulfilled by the

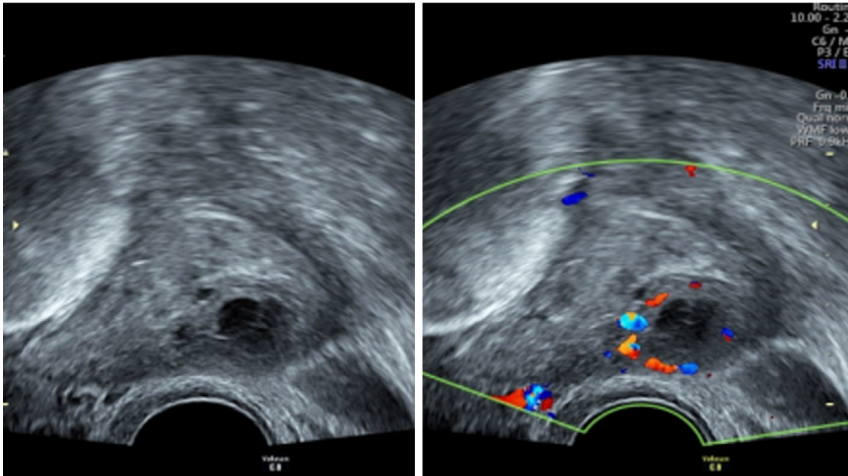


Figure 1 Transvaginal ultrasonography shows right ovarian ectopic pregnancy, with gestational sac.

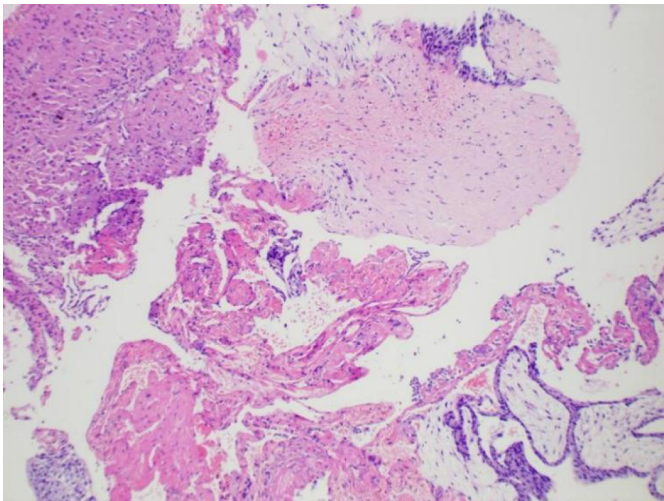


Figure 2 Photomicrograph of the right ovarian mass shows ovarian tissue with chorionic villi (hematoxylin-eosin staining, magnification $\times 4$).

present case.

A literature search yielded only nine cases of ovarian pregnancy following IUI (Table 1)[6-14]. The median patient age in these cases was 29.4 years. All 10 women (including the current patient) were primigravidae, and the ovarian pregnancies of three of these women were diagnosed preoperatively based on the presence of viable fetal heart motion. A common feature observed in these cases was ovarian enlargement due to ovulation induction, often with several hemorrhagic cysts or corpora lutea, or a certain amount of bleeding (80-2000 mL). This increases the risk of ovarian rupture, causing severe bleeding. In two cases, four to five dominant follicles were observed after ovarian stimulation, increasing the risk of ovarian hyperstimulation syndrome, which can be dangerous if accompanied by an EP. Thus, IUI treatment should be discontinued in case of more than two dominant follicles.

The pathophysiologic mechanisms underlying abnormal embryo implantation are unclear. Some theories suggest that ovarian EP could be caused by an obstruction in the release of the ovum from the ruptured follicle after intrafollicular fertilization or by embryo migration, which is related to certain conditions that damage the fallopian tube, altering tubal motility[15,16].

The risk factors for ovarian pregnancy include intrauterine device usage, pelvic inflammatory disease (PID), previous gynecologic surgery, endometriosis, sexually transmitted infections, use of ART, previous ectopic pregnancy, and salpingitis[4]. Fernandez *et al*[17] reported that ovulation induction carries an increased risk of ovarian pregnancy; during ovulation induction, the increased level of estrogen and progesterone would inhibit the peristalsis frequency of the fallopian tube and affect its

Table 1 Ovarian pregnancies following intrauterine insemination

Ref.	Age in yr	Obstetric index	Risk factors	Ovulationinduction regime	No. of dominant follicles	Gestationalage at diagnosis in wk	Rupture hemorrhage	Pregnancy at another site	Preoperative diagnosis	Treatment
El-Lakany <i>et al</i> [6]	30	G1	Ovulationinduction	HMG	2	8	800 mL	None	No	Laparoscopicoophorectomy
Bontis <i>et al</i> [7]	31	G1	Endometriosis, prior laparoscopy and ovulationinduction	HMG	2	4	No data	None	No	Laparotomy andpartial ovariectomy
Einenkel <i>et al</i> [8]	26	G1	Prior laparoscopy and ovulationinduction	Triptorelin + FSH	No data	7	80 mL	None	Yes	Laparoscopiccystectomy
Plotti <i>et al</i> [9]	34	G1	Ovulationstimulation	No data	No data	8	350 mL	Bilateral ovarian	Yes	Laparotomyand bilateralovariectomy
Kaur <i>et al</i> [10]	34	G1	Ovulationinduction	Letrozole + HMG	No data	6	No data	None	Yes	Laparoscopicresection
Shiau <i>et al</i> [11]	24	G1	Ovulationinduction	Clomiphene + HMG	5	6	1450 mL	None	No	Laparotomyand wedgerection
Goyal <i>et al</i> [12]	22	G1	Ovulationinduction	No data	No data	No data	No data	None	No	Laparotomyand excisionof sac
Gundabattula <i>et al</i> [13]	32	G1	Ovulationinduction	Tamoxifen + HMG	2	9	2000 mL	Intrauterine gestation	No	Laparoscopicresection
Eom <i>et al</i> [14]	33	G1	Ovulationinduction	Clomiphene + HMG	4	6	800 mL	Right tubal pregnancy	No	Laparoscopicresection and salpingectomy
Present case	28	G1	Ovulationinduction and pelvic adhesion	Letrozole	1	6	600 mL	None	No	Laparoscopicresection

FSH: Follicle-stimulating hormone; HMG: Human menopausal gonadotropin.

normal movement.

Several authors have reported that ART procedures increase the chance of an EP[18-20]. The ovarian pregnancy following the IUI procedure in the present case could be attributed to the higher volume of sperm suspension and a higher pressure with which it is injected into the uterus, causing backward migration of the egg to the surface of the ovary following fertilization on the ovarian surface scars from ovulation.

According to a review focused on unusual EPs[21], ovarian pregnancy is associated with PID; this condition is thought to be responsible for ovarian inflammation, which causes thickening of the tunica albuginea, reducing the follicular fluid pressure. This is speculated to cause ovulation disorder, wherein the ovum is detained in the broken follicles and fertilized just in the ovary. This pathologic process may account for the primary implantation in the ovary. Therefore, the pelvic adhesions detected during laparoscopic surgery in this case may also have been responsible for the ovarian

pregnancy. The diagnosis of PID may have been missed during gynecological examination before IUI treatment. Attention should be paid to the screening and timely treatment of PID to prevent pelvic adhesion before starting ART treatment.

Thus, close clinical follow-up, monitoring, and routine ultrasound examination are recommended after ovulation induction. In the present case, IUI after ovulation induction and pelvic adhesions may have been the causes of ovarian EP.

Early diagnosis is important to avoid more serious complications and emergency invasive surgery. It could help to understand the risk factors for EP. Transvaginal ultrasound is a valuable diagnostic method to detect early ovarian pregnancy. However, specific ultrasound features that aid a preoperative diagnosis may not always be visible. Thus, serial quantitative β -HCG levels correlated with ultrasound findings are recommended to distinguish an early intrauterine pregnancy from EP[4]. Further, early diagnosis through ultrasound examination could be difficult in women who have previously undergone ovarian induction. In fact, patients who have already undergone ovarian induction typically have enlarged ovaries and accumulated fluid in the pelvic cavity. Therefore, pelvic ultrasound should be performed more carefully in such patients. Although the ultrasound features of ovarian pregnancy were obvious in the current case, they were insufficient to establish a definite diagnosis.

Although surgery is the preferred treatment for early ovarian pregnancy, less aggressive treatment that ensures preservation of the ovarian tissue is warranted, as these patients are expected to conceive again. Laparoscopy approach should be the preferred treatment method for such patients[6,8,10,13,14].

Five of the previous nine patients were treated laparoscopically, and laparotomy was performed in the other four cases. As our patient had abdominal pain with hemoperitoneum, emergent laparoscopic resection surgery was performed; the hemoperitoneum was caused by a small mass in the right ovary, which was surrounded by a hematoma and showed minimal bleeding. The final histological examination revealed chorionic villi, confirming the diagnosis of ovarian pregnancy. Just 3 mo after surgery, the patient conceived a spontaneous intrauterine pregnancy.

CONCLUSION

In conclusion, the present case reiterates that close attention should be paid to a history of PID before IUI treatment, and patients with such a history should be closely followed up after IUI. Early measurement of serum β -HCG levels and ultrasonic examination could facilitate a timely diagnosis of ovarian pregnancy. Laparoscopic surgery could provide an exact diagnosis and enable prompt surgical intervention in these rare cases, along with preserving the ovarian tissue.

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