

## Research Letter

## Ovarian pregnancy following intrauterine insemination

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Primary ovarian pregnancy, which was first reported by Saint Maurice in 1692 [1], represents 1–3% of all ectopic pregnancies [2,3]. Its incidence after natural conception ranges from 1 in 7000 to 1 in 60,000 [2,4,5], and it remains a rare phenomenon despite the increased incidence of ectopic pregnancies following assisted conception [6]. Ovarian pregnancy occurs in the corpus luteum and often results in ovarian rupture and massive hemoperitoneum. Clinical diagnosis is tricky, and intraoperative detection requires a high index of suspicion. Several theories have been suggested to explain the ovarian implantation of the conceptus following natural conception [3,7] and *in vitro* fertilization [6–8]. Here, we report a case of ruptured intrafollicular primary ovarian pregnancy with hemoperitoneum that followed superovulation and intrauterine insemination.

A nulliparous 24-year-old woman presented to the emergency room with bilateral lower abdominal pain. She had a 2-year history of primary infertility and had been diagnosed with polycystic ovarian syndrome. She underwent two controlled, ovarian stimulation cycles induced by clomiphene citrate (Clomid; Merrel-Dow, France S.A., Neuilly-sur-Seine, France). The insufficient ovarian response prompted a third cycle with 100 mg clomiphene citrate for 5 consecutive days beginning on days 3–7 of the cycle, and two ampoules of human menopausal gonadotropin (Pergonal; I.F. Serono S.P.A., Rome, Italy) per day on days 5–9. Baseline transvaginal ultrasound (US) scan was performed at the beginning of the first treatment cycle to exclude residual ovarian cysts. US scans were repeated between days 10 and 12 of the cycle to confirm the follicular development. The scan on the night of cycle day 12 revealed three large follicles on the left ovary (mean diameter:  $17 \pm 2.1$  mm) and two large follicles on the right ovary

(mean diameter:  $18 \pm 2.2$  mm). Human chorionic gonadotropin (hCG; 10,000 IU) was administered when the mean diameter of the leading follicle reached 18 mm, and intrauterine insemination (IUI) was performed 36 hours later. Swim-up and Percoll gradients were used for sperm selection before IUI. The luteal phase was supported with 100 mg/day orally administered micronized progesterone (Utrogestan; Lab Besins-Iscovesco, Paris, France). One month after the IUI procedure, the patient was admitted to the hospital via the emergency room after having bilateral lower-quadrant abdominal pain for 1 hour. Her last menstrual period had been 1 week prior to admission; it lasted for 3 days and had been 2 weeks later than expected. On admission, her pulse was 88 beats per minute, blood pressure was 90/78 mmHg, temperature was 36.5°C, and respiratory rate was 18 breaths per minute. Her abdomen appeared distended, and there was marked rebound tenderness. A pelvic examination revealed a tender 4-cm right adnexal mass with a normal-sized uterus. Her hematocrit was 36.5%, and serum  $\beta$ -hCG level was high at 3200 mIU/mL. Ultrasonography showed a normal uterine cavity with a moderate amount of fluid in the pouch of Douglas, and no adnexal mass on the left side. On the right side, a cystic ovarian mass, 3 cm in diameter, with internal echoes, was observed. During the following hour, the patient began to show tachypnea, tachycardia, and hypotension. Subsequently, her hemoglobin decreased from an initial level of 10.3 mg/dL to 7.5 mg/dL. We suspected internal bleeding, possibly caused by an ectopic pregnancy, and performed an emergency exploratory laparotomy through a midline incision. We found massive intra-abdominal bleeding (1450 mL), a normal left fallopian tube and ovary, and an actively bleeding, blackish irregular cyst resembling a ruptured corpus luteum, 3.5 cm in diameter, in the right ovary. The cystic mass was removed by the wedge resection technique, and the edges of the remaining ovary were approximated by suturing with 3-0 chromic catgut. Histological examination identified chorionic villi attached to the ovarian tissue, which was consistent with a diagnosis of ovarian pregnancy (Fig. 1).

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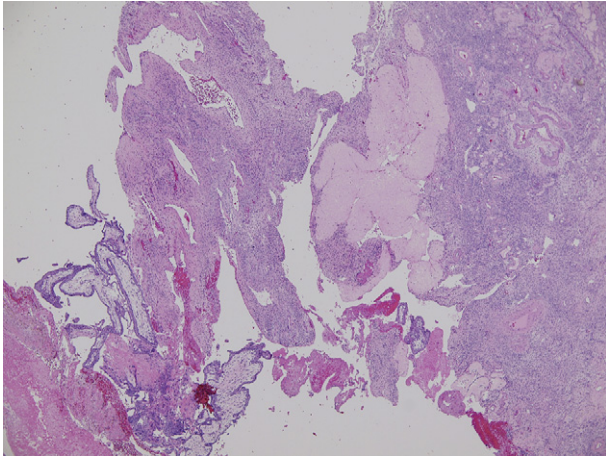


Fig. 1. Section showing ovarian tissue (O) and chorionic villi (V) (hematoxylin and eosin, 40 $\times$ ).

The postoperative course was uneventful, and the patient was discharged on the fifth day. Her  $\beta$ -hCG level progressively diminished, and she tested negative for it on day 35.

Since the first recorded instance of ovarian pregnancy in 1682, a number of patient reports, case series, and literature reviews have appeared. *In vitro* fertilization and embryo transfer are associated with an increased risk of ectopic pregnancy; the incidence ranges between 3% and 11% [9,10]. Marcus and Brinsden [6] reported that eight out of 135 (6%) ectopic pregnancies that occurred after *in vitro* fertilization were ovarian. This percentage is much higher than the corresponding percentage in naturally conceived ectopic pregnancies (<3%) [2]. One possibility is that factors that predispose patients to ovarian implantation are the same as those that cause tubal pregnancies. However, the fact that there are only three reported cases of intrafollicular ovarian pregnancy after ovulation induction/intrauterine insemination contradicts this possibility. There are several ways to explain the increased incidence of primary ovarian pregnancy after artificial reproductive techniques. Fernandez et al have reported that ovarian induction itself is associated with an increased risk of ovarian pregnancy [8]. Grimes et al have suggested that fertilization occurs normally, and implantation in the ovary occurs after reflux of the conceptus from the tube [2]. These two theories suggest that various disturbances in ovum release are responsible for ovarian implantation and that intrafollicular fertilization occurs following the failure of ovum extrusion after follicular rupture [3,7]. The occurrence of primary ovarian pregnancy following IUI may, despite its rarity, aid in understanding the pathophysiology of ovarian pregnancy. Moreover, patients with ovarian pregnancy usually are of younger age, higher parity, and exhibit fewer fertility problems than the typical pregnant woman [8]. The role of pelvic-inflammatory-disease-induced tubal damage and other causes of defective ovum release remain unclear.

It is almost impossible to diagnose ovarian pregnancy on the basis of clinical presentation alone; thus, the diagnosis is often intra- or postoperative. Marcus and Brinsden have suggested that a thick-walled cystic mass in the ovary showing internal echoes, as observed with a vaginal US scan, with or without fetal heart motion, probably indicates an ovarian pregnancy [5]. However, a hemorrhagic corpus luteum cyst also appears as an ovarian cystic mass showing internal echoes. We have found that 70% of patients with ovarian pregnancies present with intermittent lower abdominal pain, 88% with menstrual irregularity, and 48% with vaginal spotting [11]. The increased vascularity of the ovarian tissue in these cases may cause the patient to present with circulatory collapse [12]. Awareness and early detection followed by the necessary intervention can prevent complications and an adverse outcome. The current therapy for ovarian pregnancy is surgical and less invasive than in the past, which is attributable to advances in operative laparoscopy. A favorable cost–benefit ratio and the low risk of local adhesion formation make laparoscopy the approach of choice. When choosing a technique (oophorectomy versus wedge resection) for the surgical treatment of ovarian pregnancy, the more conservative methods, ovarian cystectomy and wedge resection, have distinct advantages, especially for fertile patients who wish to have children in the future.

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