

Clinical analysis of 95 cases with ovarian pregnancy

A.W. Le, Z.H. Wang, L. Shan, X.Y. Dai, T.H. Xiao, X.R. Li

¹ Department of Obstetrics and Gynecology, Nanshan Affiliated Hospital of Guangdong Medical College, Shenzhen (China)

Summary

Background: Ovarian pregnancy (OP) is a rare ectopic pregnancy, in which it is very difficult to achieve preoperative diagnosis. Ovarian blood supply in OP increases which will lead to intra-abdominal bleeding, hazarding women's lives. Surgical exploration should be conducted once cases of OP are suspected. **Objective:** To investigate clinical characteristics, diagnosis, and therapy of OP. **Materials and Methods:** A retrospective study was conducted in 95 patients with OP admitted to the present hospital from January 2005 to June 2014. **Results:** OP accounted for 1.79% of ectopic pregnancy over the same period, of which 68.4% had a history of artificial abortion, 6.3% was treated with intrauterine contraceptive device (IUD), 87.4% had abdominal pain, 84.2% had a history of menopause, and 51.6% had vaginal bleeding. All patients had no preoperative diagnosis and underwent laparoscopic wedge resection of ovary or lesionectomy and were all cured. **Conclusion:** Since the cause of OP is still unknown and it has no typical clinical manifestations, the present authors adopt blood β -hCG combined with B-ultrasound to improve the preoperative diagnosis. They prefer laparoscopic wedge resection of ovary or lesionectomy, which induce higher rate of intrauterine pregnancy and lower rates of ectopic pregnancy and infertility in re-pregnancy after surgery.

Key words: Ovarian pregnancy; Clinical characteristics; Wedge resection of ovary.

Introduction

Ovarian pregnancy (OP) is a rare kind of ectopic pregnancy with natural incidence rate of about 1 / 15,000 to 50,000, which accounts for 0.15 %~3.0% of ectopic pregnancies [1]. With the development of some birth control measures and assisted reproductive technologies, incidence of OP presents an increasing tendency. Since OP's symptoms and signs are similar to those of tubal pregnancy, it is very difficult to achieve a preoperative diagnosis. However, ovarian blood supply in OP will increase which leads to intra-abdominal bleeding, hazarding women's lives. Incidence of primary OP in patients with in vitro fertilization (IVF) is 0.3% [2]. This paper presents a retrospective analysis conducted in 95 patients with OP in the present hospital over a ten-year period, with the aim to improve awareness of the disease by analyzing the clinical data and exploring the diagnosis and treatment characteristics.

Materials and Methods

A total of 5,293 cases with ectopic pregnancy were admitted to the present hospital from January 2005 to June 2014, among which there were 95 cases with OP, accounting for 1.79%.

Clinical characteristics of the patients were the following: 1) Age range from 20 to 41 years old, (mean 27.6 ± 4.6). 2) Disease histories: 11 cases of first pregnancy, 25 cases of second pregnancy, 31 cases of third pregnancy, 23 cases of fourth pregnancy, five cases of five or more pregnancies, and one case of IVF-ET. Six cases were utilizing IUD contraception and one case had bi-

lateral tubal ligation. Sixty-five cases had histories of artificial abortion. Thirty-six cases had history of endometriosis and eight cases had received promoting ovulation drug. 3) History of menopause: 15 cases had no history of menopause and 80 cases had history of menopause, where menopause days ranged from 29 to 62 days (mean 45.6 ± 17.8). 4) Belly ache and vaginal bleeding occurred in 83 cases and 49 cases had vaginal bleeding. 5) Twenty-two cases had intra-abdominal hemorrhage more than or equal to 800 ml and 16 cases had unstable preoperative signs and required intraoperative transfusion of packed red blood cells or other plasma products. Intraoperative ruptured and unruptured ovaries were found in 43 cases and 52 cases, respectively. 6) B-ultrasound examination was performed in 95 cases and all presented ectopic pregnancy, of which 72 cases had ascites with maximum depth of 85 mm (mean 26.7 ± 15.5). 7) Colpocoeleiotomia posterior was performed in 65 cases, of which 56 cases had extracted 2~10 ml incoagulable blood. 8) Human chorionic gonadotropin (hCG) measurement was taken as preoperative routine testing of blood and were positive, with minimum value 124.8 mIU/ml, maximum value 41,337.6 mIU/ml and mean value of $7,134.7 \pm 986.6$ mIU/ml. 9) Preoperative diagnosis: all were considered ectopic pregnancy. 10) Surgery and treatment: all patients received laparoscopic ovarian wedge resection or lesionectomy.

Diagnosis was made according to criteria proposed by Spiegelberg [3]: 1) Ipsilateral fallopian tube and its umbrella end are intact and are not adhered to the ovary. 2) Embryo sac is in the ovarian tissue. 3) Embryo sac and ovary are connected to the uterus through ovarian ligament. 4) There are ovarian tissues in the embryo sac wall, confirmed histologically.

Statistical analysis

Software SPSS 16.0 was utilized for statistical analyses. The measurements are presented as mean \pm SD and compared by variance analysis. The significance of between-group differences was tested using analysis of variance or chi square tests. Values of

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$p < 0.05$ were considered statistically significant.

Results

All patients underwent laparoscopic ovarian wedge resection or lesionectomy. Examinations showed active bleeding in the rupture of ovarian surface in 23 patients, and hemoperitoneum in all patients with bleeding of 50~2,300 ml and mean of 682.7 ± 478.6 ml. Among the 95 patients, there were 58 cases with left OP and 37 cases with right OP. Intraoperative observation showed that nine cases were accompanied with pelvic endometriosis, 11 cases were accompanied with chronic pelvic inflammatory disease, and 51 cases presented pregnant corpus luteum, of which 43 cases were ipsilateral OP corpus luteum and eight cases were contralateral OP corpus luteum. One case with natural pregnancy had three gestational sacs in one ovary (Figure 1).

All surgical specimens were sent for pathological examination and were diagnosed as OP. All patients were cured and discharged from the hospital. The blood β -hCG reduced to normal level from two to four weeks after surgery.

Follow-up results: 42 of 95 cases were conducted three-year follow-up; 26 cases were pregnant at one year after surgery, of which 23 cases had intrauterine pregnancy (one case was preoperatively diagnosed as infertility) and three cases had tubal pregnancy (one case was preoperatively diagnosed as infertility). Four cases were pregnant at three years after surgery, of which two cases were diagnosed as secondary infertility. Ten cases were diagnosed as infertility prior to surgery and were not pregnant as well after surgery.

Discussion

Pathogenesis and etiology

OP is a rare gynecological acute abdomen with primary symptoms of abdominal pain. OP pathogenesis is still unclear and it may be related to the following factors: 1) It mainly occurs in women who have given birth, and it is associated with uterine cavity operation, pelvic inflammatory disease, and abdominal surgery [4]. Uterine cavity operation can cause intrauterine environment changes, such as intimal injury, which is not conducive to implantation and growth of fertilized eggs and easily leads to ectopic pregnancy. Pelvic inflammatory disease, abdominal surgery or endometriosis are likely to induce ovarian inflammation and ovulation disorders, which results in the eggs remaining within the ruptured follicle and get fertilized in the ovary. Many patients in this group had given birth, had histories of uterine cavity operation or pelvic surgery, which were likely to support these ideas. Studies [2, 3] showed that pelvic inflammatory diseases, adverse intrauterine environment, endocrine disorders, and other factors may prevent discharge of the eggs from the ovary and

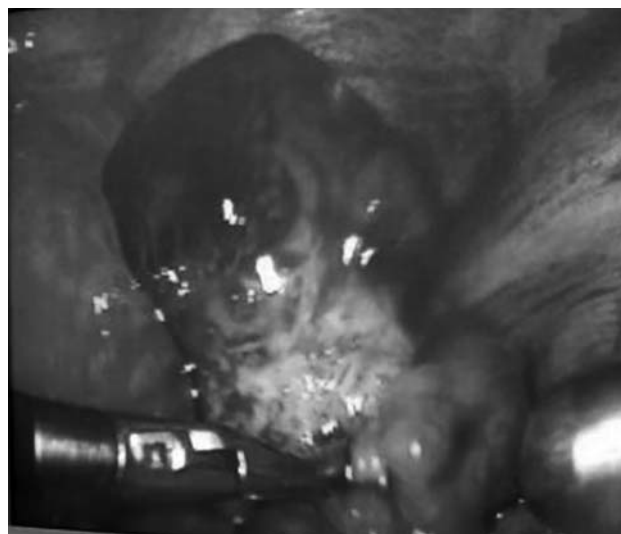


Figure 1. — Intraoperative photo of an ovarian pregnancy with three gestational sacs in one ovary.

the eggs may adhere to the ovarian surface. Then sperms may get into the surface of ovarian follicle and complete fertilization. In this study, the authors found in eight cases that the pregnant corpus luteum was located at the contralateral embryo, indicating that the fertilized eggs out-bound and implant in the contralateral ovary with unknown mechanism. Among the 95 cases, there were 58 cases with left OP and 37 cases with right OP, indicating that the incidence of left OP is significantly higher than that of the right OP, which is consistent with the previous reports with unknown reasons [5]. 2) It is associated with IUD. Sandvei *et al.* [6] indicated that the occurrence of OP in patients with IUD insertion is six times that of patients without IUD insertion, and its mechanism may be because IUD has a blocking effect on intrauterine pregnancy and tubal pregnancy, but with no blocking effect on OP. It has been reported that the blocking rates of IUD on intrauterine pregnancy and tubal pregnancy are 99.5 % and 95 %, respectively, and it has no effect on OP [7]. Studies [7] revealed that IUD can promote the secretion of prostaglandins, causing reverse peristalsis of tubal and resulting in fertilized eggs retrograde and implantation in the ovary. Meanwhile, prostaglandins may lead to dysfunction of tubal picking up eggs which further increase risks of OP. It is still controversial whether application of IUD will induce higher incidence of OP [8], although most of researchers believed that IUD insertion results in higher incidence of OP [9]. Six patients in the present study had IUD insertion, yet they could not be proven to be associated with OP. 3) Irregular maturation of follicle and ovulation failure. Relatively lower liquid pressure inside the follicle can cause ovulation disorders which results in eggs remaining in the ruptured follicle and become fertilized in

the ovary. Some researchers believed that irregular maturation of follicle during ovulation process may also result in OP [10]. The possible causes may be as follows: first, excessive estrogen leads to tubal function changes, ovulation induction drugs can result in multiple fertilized eggs and fertilized eggs may remain in the tubal during the implantation in the uterine cavity which increases the opportunity of reverse peristalsis to ovary, promoting the incidence of OP. Second, rather than being ingested into the fimbria tubae uterinae, eggs adhere to ovarian surface and fertilized after discharge from the follicle or the eggs are not discharged from the ruptured follicle and complete follicular fertilization. 4) In recent years, incidence of OP increased with the popularization and application of assisted reproductive technologies. One case in the present study had received IVF-ET. Incidence of ectopic pregnancy after IVF-ET was significantly higher than that of natural pregnancy, which is not only associated with histories of pelvic inflammatory disease, chronic salpingitis, endometriosis and operation on fallopian tube, but also related to type of embryo transplantation tube, depth into the uterine cavity, liquid volume in the tube, injection pressure, number of implanted embryos, patient's position after transplantation, development synchronization of embryo, endometrium and conditions of uterine tubal, etc [11].

Diagnosis

Due to lack of specific clinical manifestations and signs, diagnosis of OP is very difficult in early stage, and its diagnosis mainly relies on laparotomy or laparoscopy. The patients in this study had symptoms of abdominal pain, history of menopause, and vaginal bleeding with average volume of 682.7 ± 478.6 ml, indicating serious harm of OP. Therefore, early diagnosis of OP can avoid severe abdominal bleeding [12]. Some patients had no history of menopause and their abdominal pain occurred between 19 to 32 days of the menstrual cycle, which can be easily misdiagnosed as ruptured corpus luteum. In terms of imaging, theoretically, unruptured follicle may appear as an ovarian round-shaped gestational sac with thick wall, yolk sac, and embryo inside the sac by using B-ultrasound. For cases of embryo implantation in the ovarian surface, B-ultrasound may present abnormal sonographic protrusion and connection to the ovarian capsule. For cases of tubal pregnancy, B-ultrasound shows clear ovary echo and tubular structure of tuba next to the lesions [13]. Chang *et al.* [14, 15] believed that cases with gestational sac revealed in the ovarian examination by B-ultrasound can be diagnosed as OP, as well as cases with echo ball around the corpus luteum. Changes in ultrasound signs of OP are as follows: cystic mass containing part solid tissues, mixed adnexal mass accompanied by peritoneal free fluid, adnexal gestational sac, adnexal echogenic cystic mass, and gestational sac or embryo in the ovary. Foreign researchers believed that an early application of low and slow hCG combined with B-ultrasound and

increased awareness are of assistance for early diagnosis of the disease [16]. Comstock *et al.* [17] believed that ovary has characteristics of sufficient blood supply, lack of muscle tissue, and crispy texture which causes it to easily break, generating blood clots which mixes with pregnant products, ovaries, and tuba and results in blurred ovarian contour and inaccurate positioning. Preoperative diagnosis of patients in the present study all had an ectopic pregnancy.

Therapy

Patients in this study all suffered from abdominal bleeding, of which 36 cases had bleeding with a volume of ≥ 800 ml, 19 cases appeared with shock symptoms, which is associated with sufficient blood supply in ovary as well as increasing vascular number during pregnancy. Therefore, surgical exploration should be conducted once cases are suspected with an OP. The first choice is the laparoscopic surgery even if there is intra-abdominal hemorrhage. The surgical method includes removal of the gestational sac while maintaining the normal ovarian tissue as much as possible. After surgery, hCG assessment is required until it returns to normal level. After surgical therapy, most patients can conceive naturally, while very few patients may have recurrence of ectopic pregnancy or infertility [18]. For patients who want to conceive, particularly for those undergoing IVT treatment, if any tubal lesions are found during surgery, it is better to treat them as well, otherwise OP may still occur after the next embryo transplantation if the ipsilateral tubal is kept intact. Furthermore, bilateral salpingectomy may be conducted when necessary. However, salpingectomy can affect ovarian blood supply and needs comprehensive consideration. In addition, patients with abnormal fallopian tube shape can be conducted with tubal ligation if there is a high risk of ectopic pregnancy or there is a history of ectopic pregnancy.

Reports have been found on conservative medical treatment of OP in recent years, but most are case reports. For example, Cabero *et al.* [19] applied intravenous MTX. Mittal *et al.* [20] adopted intracapsular injection of MTX using laparoscopy. However, Bagga *et al.* [21] reported that even if OP is in agreement with medical treatment of ectopic pregnancy, there still may be some failed cases and may require surgery. The American Society for Reproductive Medicine Practice Committee recommends that MTX is not the preferred method for treatment of OP and OP should be confirmed by surgery [22]. Ghi *et al.* [23] believed that MTX is not the preferred method for treatment of OP. The risk of ectopic pregnancy in re-pregnancy after drug therapy is seven to 13 times greater. The rate of intrauterine pregnancy in re-pregnancy is about 50% to 80%, the rate of tubal pregnancy is 10%~25%, and the remaining include infertility [24].

Re-pregnancy results

Pregnancy prognosis was retrospectively conducted in

42 cases with OP, and the results were considered to be reasonable. Lower rates of ectopic pregnancy and infertility were achieved in re-pregnancy, indicating that the results were not poor compared with other types of ectopic pregnancy, which is consistent with the literature results [18].

In summary, preoperative diagnosis of OP is very difficult due to lack of typical clinical manifestations, relatively low incidence, and lack of exact risk factors. Patients with a history of uterine or pelvic surgery, IUD insertion, endometriosis, ovulation drug use, abdominal effusion by ultrasound, and enlarged ovary should be highly suspected to be OP and treated with laparoscopic surgery, which induces better prognosis of re-pregnancy.

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Address reprint requests to:
Z.H. WANG, M.D.
Nanshan Affiliated Hospital of
Guangdong Medical College
89 Tao Yuan Road
Shenzhen 518000 (China)
e-mail: leaiwen@126.com