CASE REPORT

Laparoscopic therapy of an intact primary ovarian pregnancy with ovarian hyperstimulation syndrome

Jens Einenkel1,3, Dieter Baier1, Lars-Christian Horn2 and Henry Alexander1

1Department of Obstetrics and Gynaecology, University of Leipzig, Philipp-Rosenthal-Straße 55, D-04103 Leipzig, Germany
2Institute of Pathology, University of Leipzig, Philipp-Rosenthal-Straße 55, D-04103 Leipzig, Germany
3To whom correspondence should be addressed at: Universitätsfrauenklinik Leipzig, Philipp-Rosenthal-Straße 55, D-04103 Leipzig, Germany.
E-mail: einj@server3.medizin.uni-leipzig.de

A case of an intact primary ovarian pregnancy with ultrasonographic demonstration of heart motion following ovarian stimulation is presented. After preoperative ultrasonographic confirmation of an extrauterine pregnancy, proof of the ovarian localization was achieved by intra-operative ultrasonographic visualization during a diagnostic laparoscopy on post-menstrual day 48. A moderate ovarian hyperstimulation syndrome with a concomitant increase in size, vulnerability and vascularity of the ovaries presented an additional challenge for the surgical approach. However, thanks to the early diagnosis of the ectopic pregnancy localization, a laparoscopic organ-preserving removal of the intact ovarian pregnancy was successfully performed. In this way, the fertility of the patient, who had previously undergone contralateral ovariectomy, was preserved. To our knowledge, this represents the first such treatment to be reported in the medical literature. Improvements in diagnosis and therapy of ovarian pregnancy are reviewed.

Key words: ectopic pregnancy/intrauterine insemination/laparoscopy/ovarian hyperstimulation syndrome/ovarian pregnancy

Introduction

Primary ovarian pregnancy is an uncommon form of ectopic implantation. Its incidence after natural conception has been reported to range from 1 in 59 740 (Boronow et al., 1965) to 1 in 4 439 deliveries (Hönigl et al., 1997), comprising up to 3.3% of all ectopic pregnancies (Raziel et al., 1990). Depending on the observation period, these values may be as high as 1 in 1 100 or 5.2% (Cabero et al., 1989).

Ectopic pregnancy (EP) is also a well known complication after IVF and embryo transfer. The increased incidence of ovarian pregnancy varies between 1 in 938 to 1 in 375 clinical pregnancies. The share of ovarian pregnancies, i.e. 1.7 to 5.9% of all ectopic pregnancies, appears unchanged (Rizk et al., 1990; Marcus and Brinsden, 1995). Higher reported incidences, such as 10%, may be explained by the small number of patients studied (Shibahara et al., 1997).

The development of an ovarian pregnancy following ovarian stimulation and intrauterine insemination (IUI) seems to be a very rare condition because to date only two cases have been reported in the literature (El-Lakany et al., 1995; Bontis et al., 1997). It is worth notice that, following ovarian stimulation, the existing problems of diagnosis and therapeutic management are considerably aggravated by the co-existence of luteal cysts in the stimulated ovaries.

This is a case report of an intact primary ovarian pregnancy following ovarian stimulation, ovulation induction and IUI. According to a MEDLINE® investigation going back to 1984, only one other case of organ-preserving laparoscopic treatment in a patient with stimulated ovaries has been described (Riethmuller et al., 1996). Our case differs in that the ovarian pregnancy was still viable, as demonstrated by means of intra-operative ultrasonographic visualization of the heart motion.

Case report

The 26 year old patient had been treated for primary sterility for one year. Her medical history was remarkable for a laparotomy at another hospital in 1998, when an ovariectomy on the right and ovarian cystectomy on the left were performed because of bilateral dermoid cysts. A diagnostic laparoscopy and dye hydropertubation showed a normal uterus and left ovary with two patent Fallopian tubes. A spermatological examination of the partner showed normal findings as defined by the World Health Organization (WHO, 1992).

Ovarian stimulation, followed by induction of ovulation and IUI, was performed in January and April 1999 but did not result in pregnancy. Another cycle of treatment was started in May 1999 (long protocol with 0.1 mg/day triptorelin, Decapeptyl®; Ferring Arzneimittel GmbH, Kiel, Germany) and 225 IU/day high-purified FSH (Fertinorm HP®; Serono Pharma GmbH, Unterschleißheim, Germany) from day 3 to 12 of the menstrual cycle). At a serum oestradiol concentration of 10 265 pmol/l, ovulation was induced with 5 000 IU of human chorionic gonadotrophin (HCG, Pregnesin®; Serono Pharma GmbH). IUI was performed on day 14 of the cycle, and luteal phase support was carried out with 3×100 mg/day progesterone (Utrogest®; Dr Kade/Besins Pharma GmbH, Berlin, Germany). Figure 1 summarizes the management and serum HCG concentrations. A solid echostructure, ~12 mm in size, with a reinforced vascular marking adjacent to the left ovary was
Regime of ovarian stimulation and course of serum human chorionic gonadotrophin (HCG) demonstrated in colour Doppler mode on day 43 of the cycle by transvaginal ultrasound scanning (7.5 MHz transducer, Logiq 500®; Kranzbühler GmbH & Co.kg). Because of the absence of a gestational sac in the uterine cavity, an ectopic pregnancy was suspected. Four days later, the ultrasound examination confirmed the diagnosis of an ectopic pregnancy, showing an echogenic ring structure ~25×20×20 mm, with a gestational sac ~14 mm in size. An embryo with heart motion, 4 mm long, was visualized adjacent to a vitelline sac, 3.5 mm in size. The left ovary measured 110×90×80 mm. The pregnancy complex could not be displaced relative to the ovary, so that an ovarian pregnancy was suspected at this early stage.

The patient suffered from minor lower abdominal pain and nausea caused by a moderate ovarian hyperstimulation syndrome, World Health Organization classification OHSS grade II (WHO, 1973). Laparoscopy was performed on day 48 of the menstrual cycle and a transumbilical 10mm port and three secondary suprapubic 5mm ports were inserted. The uterus was found to be normal (anteverted, softened, axial length 8.5 cm) and both Fallopian tubes showed normal fimbriae without dilation or collection of blood. There was no evidence of endometriosis or peritubal adhesions and no pregnancy was observed in the peritoneal cavity after thorough investigation. The left ovary was enlarged by several serous or haemorrhagic, bluish cysts and showed a smooth external surface. In the pouch of Douglas, there was ~50 ml of a serous liquid. Physiological salt solution was instilled into the peritoneal cavity allowing intra-operative vaginosonography to be performed. In this fashion, an intact pregnancy with heart motion was demonstrated within an ovarian cyst. After careful anchorage of the ovary, the ovarian pregnancy was gradually dissected by way of cystectomy using a bipolar cautery device and a triode (Figure 2). The ovarian pregnancy was removed in toto through the transumbilical port by means of an endobag. Frozen section, as well as the final histological examination, confirmed the presence of chorionic villi (Figure 3). The estimated blood loss was ~80 ml.

The patient made an uneventful post-operative recovery and was discharged on postoperative day 4. Follow-up showed a gradual decrease of HCG concentrations until a negative result (<5 mIU/ml) was obtained 3 weeks later (Figure 1).

Discussion
The case presented here is interesting in terms of both the rarity of this entity and the successful laparoscopic therapy and preservation of the stimulated ovary. Apart from several reports on ovarian pregnancies following IVF and embryo transfer (Carter and Jacobson, 1986; Rizk et al., 1990; Marcus and Brinsden, 1993; Ranieri et al., 1994; Shibahara et al., 1997) or gamete intra-Fallopian transfer (GIFT) (Lehmann et al., 1991), only two cases after IUI (El-Lakany et al., 1995; Bontis et al., 1997) have been reported so far. The common feature of all these cases is an enlargement of the ovary due to the stimulation with gonadotrophins, often with several haemorrhagic lutein cysts or corpora lutea. The increased vulnerability and vascularity of the ovary constitutes a higher risk of rupture with serious bleeding, and, possibly, haemorrhagic shock. This considerably complicates manipulation of the ovary for diagnosis and therapy during the operation, and even the localization of the pregnancy in cases without rupture may be difficult.

Even after natural conception, ovarian pregnancy still represents a diagnostic problem (Seinera et al., 1997). The symptoms
and physical findings, such as abdominal pain, menstrual irregularity, vaginal bleeding, palpable adnexal mass or hypotensive collapse, are similar to those of tubal pregnancy, haemorrhagic corpus luteum or a ruptured ovarian cyst (Van Coevering and Fisher, 1988; Raziel et al., 1990; Sidek et al., 1994; Hönigl et al., 1997). On the other hand, about 50% of ovarian pregnancies following ovarian stimulation may be diagnosed at an asymptomatic stage (Marcus and Brinsden, 1993).

Ultrasoundographically, the appearance of ovarian pregnancies varies as widely as that seen in tubal pregnancies and has been summarized recently (Hönigl and Reich, 1997). The decisive ultrasonographic characteristics for discrimination from a tubal pregnancy in the first trimester are the visualization of embryonic structures in an amniotic cavity within the ovary and, as in our case, the missing displaceability of the suspicious echostructures relative to the ovary.

Laparoscopy is now the gold standard for the diagnosis of ectopic pregnancy (Sidek et al., 1994). However, in cases with stimulated ovaries, additional diagnostic problems exist. For example, in our patient, localization of the pregnancy could only be achieved by intra-operative transvaginal ultrasonography after filling the lower pelvis with saline solution.

Because of the insufficiency of macroscopic evaluation and the risk of misdiagnosis for conditions such as a haemorrhagic corpus luteum or a ruptured, bleeding lutein cyst, histological examination is warranted even in the case of a stimulated ovary. The present case fulfils the classic anatomical and histological criteria suggested by Spiegelberg: (i) the Fallopian tubes with their fimbriae should be intact and separate from the ovary; (ii) the gestation should occupy the normal position of the ovary; (iii) the gestation should be connected to the uterus by the uterine ligament; (iv) ovarian tissue must be present in the specimen attached to the gestation sac (Spiegelberg, 1878).

Due to coagulation artefacts and the small tissue volume available, it may be difficult to find ovarian tissue around the gestational sac microscopically. A modification of the fourth postulate of Spiegelberg is the detection of chorionic villi without concurrent detection of an intact ovarian parenchyma for diagnosis and is sufficient today for a selective laparoscopic biopsy (Chelmow et al., 1994; Hönigl et al., 1997; Seinera et al., 1997).

Thus, the widely quoted classification of primary ovarian pregnancy in an intrafollicular and extrafollicular form is often not feasible. Moreover, such a classification has no therapeutic relevance. Likewise, the attempt to subdivide the extrafollicular form into juxtafollicular, interstitial, cortical and superficial types (Boronow et al., 1965) is impractical.

The therapy of early ovarian pregnancy is surgical in the first place, and in the event that the patients desire a future pregnancy, the conservation of ovarian tissue is essential. Therefore, the preferred therapeutic procedures are partial ovariectomy (wedge resection), ovarian cystectomy or blunt dissection of the trophoblast tissue. Ablative therapy such as ovariectomy or adnexectomy should be reserved for advanced cases or vital indications only.

After the first publications of a successful laparoscopic approach in the early stages of ovarian pregnancy during the late 1980s and early 1990s (Van Coevering and Fisher, 1988; Russell and Cutler, 1989; Vasilev and Sauer, 1990), laparoscopic therapy after initial diagnosis became the current method of choice (Goldenberg et al., 1994; Hönigl et al., 1997; Seinera et al., 1997). However, only one case report published to date describes a successful organ-preserving treatment by laparoscopy in a patient with stimulated ovaries (Riethmuller et al., 1996). In our case, an embryonic heartbeat could for the first time be visualized intra-operatively by transvaginal ultrasonography, proving the existence of an intact pregnancy. Thus, even an early intact ovarian pregnancy concurrent with moderate grade II OHSS is no absolute indication for laparotomy. In any case, rigorous follow-up of serum HCG concentrations is essential to detect possible persistent disease.

Only a few case reports describe medical management of ovarian pregnancy, using either methotrexate (Shamma and Schwartz, 1992; Chelmow et al., 1994), prostaglandin F2α, prostaglandin E2 and oestrogen (Koike, 1990) or mifepristone (RU 486) in combination with prostaglandin F2α (Levin et al., 1990). Because it is impossible to diagnose an ovarian pregnancy without performing at least a laparoscopy with collection of a biopsy, we agree with other authors concluding: ‘If laparoscopy is required for diagnosis, definitive surgical management may be accomplished at the same time’ (Seinera et al., 1997). Currently, taking into consideration the technological progress in endoscopic surgery, the role of medical management remains to be defined. Most ovarian pregnancies rupture in the first trimester (75–90%), with two thirds occurring during the first 8 weeks (Sandberg, 1986). In our view, non-invasive therapy, specifically with methotrexate, is only indicated as a secondary option for organ-preserving operations with a primary incomplete resection (Chelmow et al., 1994) or trophoblast persistence.

Due to a prior contralateral oophorectomy, an organ-preserving treatment was the only way of preserving fertility in our patient. In general, fertility in patients treated for an ovarian pregnancy remains unaffected and subsequent pregnancies are almost invariably intrauterine (Raziel et al., 1990; Marcus and Brinsden, 1993; Hönigl et al., 1997; Seinera et al., 1997). Until now, only one case of recurrent ovarian pregnancy (Boronow et al., 1965) and one case of tubal pregnancy after a previous ovarian pregnancy have been documented (Raziel et al., 1990).

To conclude, the present case underlines the necessity of a follow-up regimen in infertility patients treated with methods of assisted reproduction. In this way, developing complications, such as the ovarian pregnancy described here, may be diagnosed as early as possible in the asymptomatic stage. In the light of the urgent desire of these patients to become parents, organ preservation should be a primary aim, even in cases with stimulated ovaries. With further advances in minimally invasive surgery regarding surgical skills, operative technique and equipment, laparoscopy will replace conventional surgery even in such complicated situations.

Note added at proof
In the following year, the patient conceived spontaneously and visited our hospital in June, 2000, 11 months after the operation. Ultrasonographic examination revealed an inconspicuous intrauterine pregnancy at 8 weeks gestation.
References


Received on 17 February 2000; accepted on 14 June 2000