

CASE REPORT

Uterine rupture in first or second trimester of pregnancy after in-vitro fertilization and embryo transfer

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We report five cases of early rupture of cornual pregnancy with history of previous salpingectomy and cornual resection following in-vitro fertilization (IVF) and embryo transfer. We discuss the predisposing factors, diagnostic and therapeutic modalities in these patients. A high index of suspicion is required for an early diagnosis. It is imperative that the physicians who care for the patients be fully aware of the possibility of such a complication in a high risk population; therefore, appropriate counselling and close follow-up might help to avoid such obstetrical catastrophes, by termination of pregnancy, either surgically or medically.

Key words: cornual pregnancy/in-vitro fertilization/placenta percreta/salpingectomy/uterine rupture

Introduction

Spontaneous uterine rupture early in the course of pregnancy is a rare complication in patients treated by in-vitro fertilization (IVF) and embryo transfer. The risk of uterine rupture exists when there is an associated uterine and/or placenta factor. Here, we report five cases of uterine rupture in the first and second trimester of pregnancy.

Case 1

A 25 year old woman consulted our IVF centre with a 3 year history of primary infertility. Her past history included two spontaneous abortions in 1991, two ectopic pregnancies in 1992, treated by bilateral salpingectomy with left cornual resection. Her infertility work-up revealed mild endometriosis and hyperprolactinaemia. In 1993 the patient was enrolled in an IVF cycle, and received a stimulation protocol including gonadotrophin-releasing hormone agonist (GnRHa) and follicle stimulating hormone (FSH). IVF/embryo transfer was performed after transvaginal ultrasound-guided follicular aspiration.

A left cornual pregnancy was suspected following transvaginal ultrasound 5 weeks after embryo transfer. The patient was hospitalized 3 weeks later because of severe haemorrhagic

shock without vaginal bleeding or cervical changes. An emergency laparotomy was undertaken and a fetus was found under the parietal peritoneum. A vertically ruptured uterus at its left side was found, but this rupture was fortunately limited by a left ovarian adhesion which rendered haemostasis less difficult. The uterus was repaired in two layers after adhesiolysis. The trophoblastic adhesions were noted on some of the intestinal loops. Pathological examinations of embryo and placenta were normal.

Case 2

A 34 year old patient with a 6 year history of secondary infertility was referred to our centre in 1987. She had conceived spontaneously 9 years earlier and delivered a healthy infant boy weighing 4100 g. In her past history, she had two ectopic pregnancies treated by left salpingectomy with cornual resection and right partial salpingectomy in 1981 and 1982 respectively. In 1983, the right Fallopian tube was reconstructed. Three attempts at IVF/embryo transfer in 1986, 1987 and 1991 resulted in two ectopic pregnancies (1986 and 1991) managed by right salpingotomy and one spontaneous abortion (1987). In 1993, she underwent a right salpingectomy for her fifth ectopic pregnancy following a spontaneous conception. In 1994, controlled ovarian stimulation was induced using GnRHa and FSH for her fifth IVF attempt, which resulted in conception.

At the eighth week of gestation, a heterotopic pregnancy, with one embryo in the right cornual region and another in the uterine cavity, was suspected following transvaginal ultrasound. This finding was confirmed at the 12th week and laparoscopy was undertaken 2 days later. However, only a haemorrhagic cyst in the right ovary was discovered. The patient was admitted for severe abdominal pain and pre-shock state 1 week later. Laparotomy was performed and revealed a massive haemoperitoneum and a right-sided uterine cornual rupture due to *placenta percreta*, with one fetus and placenta in the abdominal cavity and the second fetus in the uterus. The left ovary was buried under the adhesions between the intestinal loops and uterus. After adhesiolysis of sigmoid from uterus and right ovary, total hysterectomy with left oophorectomy was performed. Each of the two fetuses weighed about 30 g, with a crown-rump length of ~7 cm. The presence of *placenta percreta* and normal fetuses was confirmed by pathological examination.

Case 3

A 33 year old patient with a history of two early spontaneous abortions and right salpingectomy in 1987 and 1988, Caesarean section for premature delivery with breech presentation in 1990 and left salpingectomy with cornual resection in 1992, was referred to our centre for secondary infertility of 2 years' duration. Our diagnostic work-up revealed adenomyosis, and the patient was treated by GnRHa for 6 months. IVF was performed, serial serum β -human chorionic gonadotrophin (HCG) determination and ultrasound examination confirmed the presence of pregnancy following transfer of thawed cryopreserved embryos, in 1994.

At 18 weeks gestation, she was hospitalized for a vaginal bleeding and abdominal pain, while an ultrasound examination revealed a fetus with cardiac activity. Laparoscopy was undertaken, and led to an emergency laparotomy because of haemoperitoneum. A living fetus with intact membrane in the left cornual region of uterus and a transverse rupture of uterine fundus was discovered which was repaired in two layers. Pathological examination showed a normal fetus and placenta.

Case 4

A 25 year old infertile woman was referred to our centre for IVF/embryo transfer, in 1987. She had previously undergone bilateral salpingectomy and cornual resection following left ruptured tubal pregnancy and right hydrosalpinx, in 1986. Ovulation was induced by clomiphene citrate and human menopausal gonadotrophin (HMG). After oocyte retrieval and IVF/embryo transfer, the presence of pregnancy was confirmed by serial serum β -HCG determinations; 6 weeks later, ultrasound study showed two gestational sacs and the fetal beating hearts. Spontaneous abortion of one of the fetuses occurred 5 weeks later, manifested by vaginal bleeding, and subsequently a single pregnancy continued.

At 20 weeks gestation, she was admitted to the emergency service with abdominal pain and clinical signs of shock without vaginal bleeding. Haemoperitoneum and fetal death were discovered by ultrasonography, and thus the patient underwent an emergency laparotomy. At the time of operation, the fetus was found in a blood-filled abdominal cavity and a transverse rupture of uterine fundus was found. Evacuation of gestational contents was performed through the uterine defect and the uterus was repaired in two layers. Pathological examination confirmed a normal fetus and placenta.

Case 5

A 27 year old woman with a 5 year history of primary infertility was referred to our institution for IVF/embryo transfer. Her past history included a bilateral salpingectomy and cornual resection in 1984. In 1990, the patient underwent a long protocol using GnRH and HMG (Bouliou *et al.*, 1988) for ovulation induction. Serial β -HCG determinations and transvaginal ultrasound revealed an intact intra-uterine twin pregnancy 5 weeks after embryo transfer.

At 26 weeks gestation, she was hospitalized because of an intense abdominal pain and haemorrhagic shock. Ultrasound

study revealed haemoperitoneum with no visible fetal heart activity. An emergency laparotomy was undertaken. A ruptured uterus in its right cornual region along with haemoperitoneum was discovered. Two girl fetuses of 840 g and 680 g without any anomaly were extracted from the abdominal cavity. Both placentas were situated in the right cornual region of the uterus. Total hysterectomy was performed. Histological examination of the surgical specimens confirmed *placenta percreta* as a predisposing cause of uterine rupture.

Discussion

Early uterine rupture is a rare condition which occurs essentially in a scarred uterus [e.g. deep cornual resection, myomectomy (Dubuisson *et al.*, 1995), Caesarean section, iatrogenic uterine perforation]. Other less common causes are placenta increta, congenital anomalies, trauma, and sacculation of entrapped retroverted uterus. Among these aetiologies, *placenta percreta* although rare, is a highly morbid situation. It is usually manifested in the third trimester with only rare cases reported earlier, and usually diagnosed intraoperatively. The conditions which predispose to invasive placentation include a previous dilatation and curettage, uterine scarring, advanced maternal age and previous endometritis. These risk factors are frequently seen in the IVF/embryo transfer candidates.

From 1987 to 1994, 3789 IVF cycles were performed in our centre, which led to 786 pregnancies. All of the five reported cases (0.6%) which were complicated by uterine rupture had a past history of salpingectomy with or without cornual resection. Routinely in our centre, the patients are followed, after their conception, by their gynaecologists outside of our institution. It is believed that the salpingectomy with cornual resection attenuates uterine musculature at the cornual region which can lead to a subsequent rupture of the uterus in the early course of pregnancy. Likewise, the presence of *placenta percreta* in the cornual region in two of our patients, as well as adenomyosis, twin pregnancy in two others (presence of heterotopic pregnancy (Beck *et al.*, 1990; Pangui *et al.*, 1993) and *placenta percreta* in case 2), seems to be a predisposing cause for earlier rupture in the course of pregnancy.

Close observation is required for the susceptible patients with single or multiple predisposing factors. Ultrasonography is of great value in earlier diagnosis of unusual pregnancy location, thin uterine wall and adherent placentation. Cornual pregnancy may be diagnosed according to three sonographic criteria: (i) an empty uterine cavity; (ii) a chorionic sac seen separately and >1 cm from the most lateral edge of the uterine cavity; and (iii) a thin myometrial layer surrounding the chorionic sac (Timor-Tritsch *et al.*, 1992).

Rupture in this area is potentially catastrophic and hysterectomy is often necessary because of the excessive disruption of uterine tissue. The earlier diagnosis of an unruptured cornual pregnancy may allow a conservative approach without additional risk to the patient. The classical treatment of cornual pregnancy is surgical, either cornual resection with simple suture repair of the lesion or hysterectomy. Conservative surgical management of cornual pregnancy includes treating by

hysteroscopically guided curettage under laparoscopic control (Meyer and Mitchell, 1989), conservative management with preservation of tubal architecture (Confino and Gleicher, 1989) and laparoscopically-directed intervention (Gleicher *et al.*, 1994). Cornual pregnancy may also be treated successfully by medical treatment such as methotrexate (MTX) (Tanaka *et al.*, 1982). Non-surgically transvaginal sonographic puncture with injection of MTX or potassium chloride (KCl) (Porreco *et al.*, 1990) is another method of conservative treatment of cornual pregnancy (Menard *et al.*, 1990; Timor-Tritsch *et al.*, 1991; Venezia *et al.*, 1991).

Therefore, one can conclude that cornual-interstitial pregnancies in selected cases can be treated with less invasive approaches than salpingectomy and cornual resection or hysterectomy.

In suspected cases of *placenta percreta*, particularly in the presence of an unexplained maternal serum α -fetoprotein elevation (Ginsberg *et al.*, 1992; Zelop *et al.*, 1992; Kupfermanc *et al.*, 1993), sonographic examination has an important role in diagnosis (disappearance of the retro-placental anechogenic zone); other imaging modalities such as colour Doppler sonography (Rosemond *et al.*, 1992) and magnetic resonance imaging (Throp *et al.*, 1992) have been proposed. Physicians counselling patients should maintain an awareness of its existence in patients with acute abdomen in pregnancy. Early diagnosis of *placenta percreta* can alter approach and outcome, decreasing maternal mortality and morbidity. Conservative therapies such as leaving the placenta in place, localized resection and uterine repair and oversewing of the uterine defect, may still be viable alternatives to hysterectomy when blood loss is not excessive, and preservation of fertility is desired (Cox *et al.*, 1988).

In conclusion, regarding the higher incidence of the above-mentioned risk-factors of uterine rupture in IVF candidates, ultrasound study for diagnosis of the site of gestational sac and placentation, and colour Doppler and maternal serum α -fetoprotein measurements in doubtful cases of *placenta percreta* seems necessary, since early diagnosis renders conservative treatment possible.

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