Heterotopic triplet pregnancy: report and video of a case of a ruptured tubal implantation with living embryo concurrent with an intrauterine twin gestation

Flávio Garcia Oliveira received his MD degree with distinction in 1981 from the School of Medicine of Ribeirão Preto at the University of São Paulo (Brazil). After completing his residency in 1984, he trained in private practice of obstetrics and gynaecology in the state of Paraná (Brazil), where he started his own practice of laparoscopy/hysteroscopy in 1988. He joined the unit of gynaecological endoscopy of the Clínica e Centro de Pesquisa em Reprodução Humana ‘Roger Abdelmassih’ in São Paulo in 1995. There, he is currently senior consultant. He is a member of the Brazilian Society of Human Reproduction and Menopause. His interests are technologies applied to infertility evaluation, especially laparoscopy/hysteroscopy, and high-risk pregnancies, especially from assisted reproduction procedures.

Dr FG Oliveira

Flávio Garcia Oliveira¹, Vicente Abdelmassih, Soraya Abdelmassih Oliveira, Roger Abdelmassih, Zsolt Peter Nagy
Clínica e Centro de Pesquisa em Reprodução Humana ‘Roger Abdelmassih’, Rua Maestro Elias Lobo, 805, 01433-000, São Paulo-SP, Brasil
¹Correspondence: Tel: +55 11 38871555; Fax: +55 11 38858607; e-mail: flaviogo2@uol.com.br

Abstract

This report presents a case of triplet heterotopic gestation after intracytoplasmic sperm injection (ICSI)-IVF treatment, with a left ruptured ectopic tubal implantation with a living embryo and successful outcome of the concurrent intrauterine twin gestation. A couple whose infertility was caused by oligoasthenozoospermia was referred for ICSI treatment. Three good quality embryos were transferred at the request of the patient. Early gestational control was performed by ultrasound at weeks 5 and 7 of gestation. The patient reported to the centre during week 7 with severe abdominal pain and with signs of peritoneal irritation. Transvaginal ultrasound revealed an extra-uterine ruptured implantation. During the concomitantly performed laparoscopic procedure, a living embryo was observed after opening the extra-uterine embryonic sac. Heartbeat activity was present and lasted for 5 min after surgical resection of the tubal implantation. The patient was discharged from hospital without complications. The intrauterine twin gestation was not affected and two healthy infants were born at week 38 of gestation. Heterotopic pregnancy should be ruled out in patients submitted to IVF–embryo transfer, although no predisposing factors are present in some cases. Precise diagnosis may be delayed due to some important characteristics of the IVF–embryo transfer treatment. Nevertheless, this condition should be diagnosed by ultrasound before tubal rupture to avoid obvious complications. Laparoscopy remains the gold standard for diagnosis and treatment in these cases. The presentation of the heterotopic pregnancy was recorded on video and may be viewed on the internet at www.rbmonline.com/Article/710.

Keywords: embryo, heterotopic gestation, ICSI, laparoscopy, transvaginal ultrasound

Introduction

The incidence of natural heterotopic pregnancy (HP) is close to 1/30,000 pregnancies. This rate increases dramatically among women undergoing induction ovulation treatments and assisted reproductive technologies. Rates of 0.75–3% have been reported after IVF with embryo transfer and they are increasing in line with a rise in the incidence of multiple gestations after IVF–embryo transfer (Tal et al., 1996). Predisposing factors include the presence of pelvic pathologies, higher volume of transfer medium in the catheter and large number of transferred embryos (Verhulst et al., 1993; Tummon et al., 1994).

Several cases of heterotopic pregnancy have been reported in recent years and the site of the ectopic implantation is similar to primary ectopic pregnancies. Most cases are tubal implantations, although abdominal, cervical and ovarian heterotopic pregnancies with successful outcomes of the intrauterine pregnancies (IUP) have also been described (Baker et al., 1997; Shahabuddin et al., 1998; Oliveira et al., 2001). Ultrasonographic technologies, especially transvaginal probes, have facilitated early diagnosis of heterotopic and ectopic pregnancy. Laparoscopy has become the preferred method for diagnostic confirmation of heterotopic pregnancy, and is a safe surgical procedure to treat this condition (Pistofidis et al., 1995; Wang et al., 1998). In this case report, the interesting clinical presentation, pathophysiology and therapeutic and diagnostic approaches are discussed. The presentation of the heterotopic pregnancy was recorded on video.
**Figure 1.** Seven week gestational sac. This image was obtained before opening the gestational sac on a ruptured left tubal implantation from a heterotopic triplet pregnancy with intrauterine twin gestation. The video presentation may be viewed on the internet at www.rbmonline.com/Article/710.

**Figure 2.** Seven week embryo with heartbeats. This image was obtained after opening the gestational sac on a ruptured left tubal implantation from a heterotopic triplet pregnancy with intrauterine twin gestation. The video presentation may be viewed on the internet at www.rbmonline.com/Article/710.
Case report

A 31-year-old woman and her husband (who had oligoasthenozoospermia) were treated by IVF-intracytoplasmic sperm injection (ICSI). No abnormalities were found in her routine investigation, which included general and gynaecological examinations, transvaginal sonography and hysterosalpingogram.

Twelve oocytes were recovered from the patient after ovarian stimulation. Six MII oocytes were injected and three good quality embryos were transferred to the patient on day 3.

Twelve days after the transfer, the serum b-human chorionic gonadotrophin (hCG) concentration (fluorimunnoassay; Delfia, Wallac Oy, Turku, Finland) was 432 mIU/ml. Early follow-up ultrasound was performed once a week, starting on day 24 after transfer. During this period, the patient was asymptomatic and the ultrasound examination was falsely reassuring, showing intrauterine twin gestation without signs of a third implantation. On day 38 after transfer, the patient reported to the centre with severe abdominal pain, abdominal distension and peritoneal irritation signs. Transvaginal ultrasound examination detected two well-positioned gestational sacs in the uterine cavity, with living embryos (heartbeats = 171 bpm, and crown–rump length = 14.5 mm). The ovaries had bilaterally enlarged volume with multiple luteal cysts. A third gestational sac with a living embryo (heart beats = 168 bpm and crown–rump length = 14 mm) was also observed on the left uterine adnexa. A moderate quantity of echogenic fluid was present in the pouch of Douglas. The patient was advised of the potential seriousness of her pathological condition. She was also informed about the necessary diagnostic examinations and about the best approach to resolve the condition. The patient understood and consented to all necessary diagnostic and treatment interventions.

A diagnostic laparoscopy was performed under general anaesthesia, in which a haemoperitoneum of approximately 1000 ml was detected. The ruptured heterotopic pregnancy on the left tube was treated successfully with laparoscopy. After salpingectomy, the gestational sac was opened and a living embryo with heart beats was observed (see time-lapse film – accessible from icon below abstract on previous web page). Heart beat activity lasted for 5 min after interruption of the septic pump. A living embryo at the ectopic site was observed for 5 min. The pathophysiology of heterotopic pregnancy is unknown. It is possible that the embryo reaches the ectopic site during the transfer because of the propulsive forces applied to the medium in the catheter, or immediately thereafter through the intrinsic uterine transport mechanisms. The uterus and Fallopian tubes represent a functional unit with regard to transport of spermatozoa. For this reason, one may suppose that a similar mechanism can regulate transportation of cells and substances from the vagina and uterine cavity up to the tubes, including embryos. The uterus seems to act as a peristaltic pump that provides the pressure gradients necessary to transport spermatozoa from the vagina to the Fallopian tubes. A functional sphincter mechanism located in the area of the utero–tubal junction that is actively relaxed by secretory products originating from the ovary bearing the dominant follicle allows further transport to the ampullary part of the tube on the side of the follicle destined to ovulate, while the contralateral oviduct remains functionally closed. This mechanism of transport is not observed during the early luteal phase in normal patients (Wildt et al., 1998). Although evidence is scarce, alteration of this mechanism may cause abnormal transport of embryos to the tubes after transfer. This may be due either to controlled hyperstimulation of the ovaries causing an abnormal secretory milieu in each utero–tubal junction and allowing both tubes to open for transportation (in general there are several follicles in both ovaries), or to a defective mechanism of transportation caused by tubal pathology where local mediators or oxytocin could be liberated and induce such a defective mechanism. This may be a factor in some cases of bilateral tubal ectopic pregnancies (primary and heterotopic) and in the higher incidence of ectopic pregnancy observed in patients who have had tubal disease.

On day 38 after transfer, the patient reported to the centre with severe abdominal pain, abdominal distension and peritoneal irritation signs. Most HP cases are asymptomatic until week 7, and the clinical presentation is extremely inconsistent (Shahabuddin et al., 1998).

This patient had a serum β-hCG concentration of 432 mIU/ml on day 12 after transfer, which suggested a multiple gestation even before the first control ultrasound. There is an association between higher β-hCG concentrations on day 12 after transfer (>400 mIU/ml) and the development of multiple pregnancies (Schmidt et al., 1994).

The presence of the intrauterine pregnancy (IUP) may disguise the initially slowly increasing curve of β-hCG concentrations associated with primary ectopic pregnancies. This fact, together with the presence of multiple luteal cysts in the ovaries, may delay the diagnosis of HP. Moreover, the presence of more than one intrauterine gestational sac is not indicative of the final number of implantations. During ultrasound examination, the adnexa should be carefully evaluated, even if an intrauterine gestational sac is already present. Both physicians and patients should be made aware that the existence of an IUP does not preclude the risk of ectopic implantations. Unfortunately, in the present case, diagnosis of this condition was not made earlier; however, it was possible to preserve the IUP through a timely laparoscopic procedure. As the present case demonstrates also, laparoscopy remains the gold standard for therapeutic interventions in HP.
cases (Einenkel et al., 2000), and to improve IUP outcomes. Successful IUP outcomes until term represent ~65% of HP cases today (Tal et al., 1996).

In the present case, the patient was advised that a maximum of two embryos should be transferred; however, the couple insisted on the transfer of three embryos. One should be cautious about the number of transferred embryos, especially if they are of good quality (<5% fragmentation and >7 cells on day 3) and when they are being transferred to a younger patient.

Finally, it was novel to observe the relatively long (~5 min) heart activity of the embryo after interruption of the tubal circulation. No descriptions have been found in the literature regarding the time of survival of an embryo in this situation. The present observation may demonstrate that the trophoblast function was good, a factor linked to the high quality of this embryo and its membranes. On the other hand, this observation may demonstrate that the initial trophoblast circulation has some reserve of nutrients and oxygen to maintain the vitality of the embryo for a few minutes without any influx of blood. In the last 15 years of experience in endoscopic surgery, this was the first observation of a living embryo that survived a few minutes after resection of the ectopic implantation.

Further improvement in the outcome of HP cases will come mainly from increased clinician awareness and early invasive diagnostic and therapeutic techniques. Care should be taken regarding the number of good quality embryos transferred to younger patients, because of the higher risk of multiple implantation and consequently heterotopic gestation. It is recommended that detailed ultrasound studies, preferably via the vaginal route, should be performed on patients in assisted reproductive technology programmes.

References


Oliveira FG, Abdelmassih V, Balmaceda JP et al. 2001 Two rare cases of ovarian pregnancies (heterotopic and primary ectopic) after intracytoplasmic sperm injection (ICSI) and blastocyst transfer. Human Reproduction 16, 2227–2229.


