Case Reports in Women's Health 22 (2019) e00106

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

In-vitro fertilization resulting in heterotopic pregnancy, ovarian hyperstimulation and paralytic ileus: A case report

Vedran Madžarac [a,*], Željko Duić [a,b], Josip Valetić [a], Gordana Planinić-Radoš [a]

[a] Department of Obstetrics and Gynecology, University Hospital Merkur, Ivana Zajca 19, 10000 Zagreb, Croatia
[b] Medical school, University of Zagreb, Šalata 3b, 10000 Zagreb, Croatia

ARTICLE INFO

Article history:
Received 31 January 2019
Received in revised form 3 March 2019
Accepted 7 March 2019

Keywords:
Heterotopic pregnancy
Ovarian hyperstimulation syndrome
Paralytic ileus
In-vitro fertilization

ABSTRACT

Heterotopic pregnancy followed by ovarian hyperstimulation syndrome and paralytic ileus are rare and potentially fatal complications associated with assisted reproduction. A 37-year-old nulliparous woman, after in-vitro fertilization and embryo transfer, presented to the gynaecology department with severe abdominal distension, diffuse abdominal pain and vaginal bleeding. Transvaginal ultrasound examination revealed an intrauterine pregnancy, with both ovaries enlarged, measuring 10cmx10cm, with free fluid in the pouch of Douglas. Another gestational sac was visualized in the left adnexal region with a viable pregnancy, crown–rump length (CRL) 6.6 mm at 6 weeks of gestation. Left salpingectomy via laparotomy and uterine evacuation were performed. The patient's postoperative course was complicated by the development of ovarian hyperstimulation syndrome and paralytic ileus. The patient recovered well after receiving supportive therapy. Clinicians should always be aware of the complications associated with assisted reproductive techniques.

1. Introduction

Heterotopic pregnancy is defined as intrauterine pregnancy coexisting with an ectopic gestation. Its incidence in the general population is around 1 in 30,000 pregnancies, but it is more common in patients undergoing assisted reproduction. In rare cases, heterotopic pregnancy may be accompanied by ovarian hyperstimulation syndrome (OHSS), which is a well recognized occurrence after in-vitro fertilization (IVF). The incidence of both OHSS and heterotopic pregnancy has increased in recent years as a result of the greater number of pregnancies achieved by assisted reproductive techniques (ART). We present a case of OHSS and heterotopic pregnancy after IVF and embryo transfer complicated by postoperative paralytic ileus.

2. Case Report

A 37-year-old nulliparous woman with a 10-year history of primary infertility presented to the gynaecology department 30 days after embryo transfer, complaining of severe abdominal distension, diffuse abdominal pain and vaginal bleeding. Ovulation was induced by gonadotropin-releasing hormone (GnRH) agonist. Human chorionic gonadotropin (hCG) was administered as luteal-phase support seven days after the transfer of two embryos. At hospital admission, the patient was found to have a diffusely painful distended abdomen without guarding or rebound. Pelvic examination revealed vaginal bleeding coming from a closed cervix, accompanied by a soft enlarged uterus, and bilateral tender masses could be felt in the adnexal region. On laboratory testing her haemoglobin level was 10.5 g/dL, white blood cell (WBC) count 31.8 $\times 10^9$/L and haematocrit 54%. The serum hCG level was 70,128 IU/L. An initial transvaginal ultrasound examination revealed a viable intrauterine pregnancy. Both ovaries were enlarged, measuring 10 cm $\times$ 10 cm, with multiple cysts measuring up to 3.5 cm in diameter. Free fluid in the pouch of Douglas was also present. Due to a gradual increase in vaginal bleeding and more intense abdominal pain reported by the patient, a repeat transvaginal ultrasound scan was done, which showed only irregular echoes in the uterine cavity, and so miscarriage was diagnosed. Additionally, and unnoticed at the first ultrasound examination, a viable ectopic pregnancy (crown–rump length 6.6 mm at 6 weeks of gestation) in the ampullary region of the left fallopian tube was found (Fig. 1). Instead of a laparoscopic approach, laparotomy was performed in light of the severe abdominal distension and considerable bilateral ovarian masses. The ultrasound finding was confirmed, with an ectopic pregnancy in the ampullary part of the left fallopian tube. Both ovaries were enlarged, with multiple cysts caused by ovarian hyperstimulation. There was approximately 300 mL of clotted blood in the pouch of Douglas. Left salpingectomy and uterine evacuation were performed. Ectopic gestation was confirmed on pathology examination of the removed fallopian tube and products of conception in the intrauterine tissue sample.

* Corresponding author.
E-mail addresses: vmadarac@gmail.com (V. Madžarac), zeljko.duic3@zg.t-com.hr (Ž. Duić).

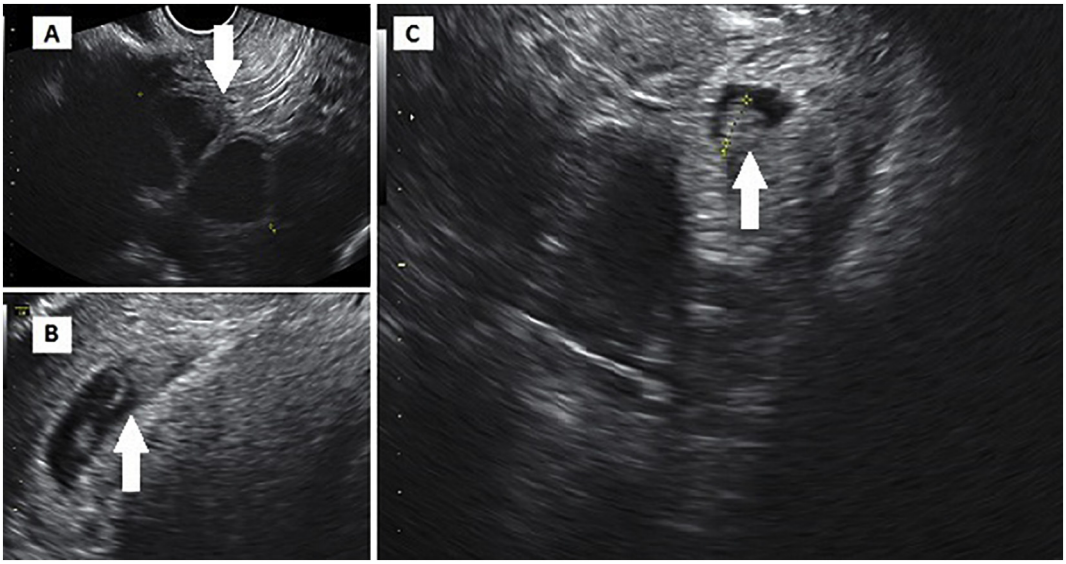

Fig. 1. Transvaginal ultrasound images of heterotopic pregnancy and ovarian hyperstimulation: (A) enlarged left ovary with multiple cysts measuring 10 cm × 10 cm; (B) mass of mixed echogenicity in the uterine cavity; (C) gestational sac in the left adnexal region with viable pregnancy, crown–rump length (CRL) 6.6 mm at 6 weeks of gestation.

Postoperatively, the patient's condition was stable for the first 24 h but then the ovarian hyperstimulation worsened and she developed oliguria and further abdominal distension. A significant increase in ovarian size was noted: that on the right now measured 12 cm × 10 cm and that on the left 11 cm × 9 cm. The free fluid in the pouch of Douglas was observed to have increased in volume and to have spread throughout the abdomen. There was elevation of the WCC (57.1 × 109 /L) and the estradiol (E2) level had risen above 4000 pg/mL, making clear the diagnosis of OHSS.

The patient was managed with intravenous fluid intake, 100 mL of 20% albumin and thromboprophylaxis with low molecular weight heparin. Over the next few days, the patient's clinical condition improved, but on the fourth postoperative day she started to complain of abdominal pain with bloating, further abdominal distension with no bowel movements or bowel sound. On abdominal ultrasound, dilated bowel loops were found, without bowel activity; a diagnosis of paralytic ileus was confirmed by abdominal X-ray. There was no signs of bowel or uterine injury.

The patient received supportive therapy, including nasogastric tube, nutritional support, fluid replacement, low molecular weight heparin and stimulation of bowel movement (erythromycin 250 mg and neostigmine 1.5 mg/day). Two days later she developed bowel movement and recovered. She was discharged from hospital two weeks after admission.

3. Discussion

Advances in ART and more frequent use of ovulation induction have resulted in an increased incidence of iatrogenic pregnancy complications, including heterotopic pregnancies and OHSS, as described in this case. Previous tubal surgery, endometriosis as well as pelvic inflammatory disease are all considered to be risk factors for heterotopic pregnancy, in addition to ART, which is now considered to be the most important one.

The moderate and severe forms of OHSS have been found in approximately 3% of all gonadotropin ART cycles [1]. It is important to recognize the possibility of OHSS if there are rapidly rising estradiol levels and a high antral follicle count, since in these situations the OHSS can be prevented. Cycle cancellation by withholding the hCG trigger, temporarily stopping gonadotropin administration and postponing the hCG trigger until the estradiol level is lower, agonist trigger, and cryopreservation are all reported to be effective strategies [2]. Ovarian hyperstimulation in ART causes a luteal-phase defect with reduced progesterone production. One of the strategies associated with a higher rate of live births in ART procedures is administration of hCG for luteal-phase support; however, this may result in higher rates of OHSS [3].

Heterotopic pregnancy still represents a diagnostic challenge, despite advances in technology. Ultrasound visualization of an intrauterine pregnancy and its normal production of hCG may often give false reassurance. Pelvic ultrasound as the gold standard should be performed by an experienced ultrasonographer in all cases when more than one embryo was returned after ART and if symptoms are suggestive of an ectopic pregnancy, despite visualization of an intrauterine pregnancy (whether normal or abnormal). In a retrospective study of 25 heterotopic pregnancies by Yu et al., 56% of cases were diagnosed by a routine transvaginal ultrasound examination at 6–7 weeks of gestation. The remaining 44% of cases were identified on repeat ultrasound after the patient had become symptomatic [4]. Early diagnosis of heterotopic pregnancy in the setting of OHSS is even more difficult. Visualization of the adnexal region is often compromised by enlarged, multicystic ovaries. Clinical symptoms such as lower abdominal pain and vaginal bleeding are not reliable since they are often misinterpreted as symptoms of OHSS. Giurgis et al. found that most cases of heterotopic pregnancies complicated by OHSS are diagnosed only at laparotomy [5].

Surgical removal of heterotopic pregnancies can be performed via laparotomy or laparoscopy with minimal manipulation of the gravid uterus. In heterotopic pregnancies accompanied by OHSS, a poor operative field can be expected, and so laparotomy is the recommended approach. However, after the surgery the potentially fatal complication of paralytic ileus can develop, as in our case. The pathophysiology of paralytic ileus is not fully understood. Groups of hormones and neurotransmitters, including nitric oxide, vasoactive intestinal peptide and substance P, have been identified as factors contributing to paralytic ileus via inhibitory action on the gastrointestinal tract. Recently, a reduction in gastrointestinal blood flow mediated by vascular endothelial growth factor (VEGF) – a key element of OHSS pathophysiology - was identified as a potential cause of paralytic ileus [6].

A good perinatal outcome for the intrauterine part of a heterotopic pregnancy can be expected according to most studies [4,7]. In a study by Svare et al., nine of 13 intrauterine pregnancies resulted in term deliveries [8]. The perinatal outcome of an intrauterine pregnancy in the setting of moderate or severe OHSS is difficult to estimate, due to lack of data and the rarity of such cases.

This case highlights the importance of close surveillance of patients after induction of ovulation. The risk of complications such as OHSS and ectopic pregnancies can be reduced by inclusion of effective preventive strategies in IVF protocols. Paralytic ileus can be considered a rare and potentially fatal manifestation of severe ovarian hyperstimulation. If criteria are met, non-surgical treatment of heterotopic pregnancy can significantly reduce the risk of paralytic ileus, especially in the setting of OHSS.

Contributors

Vedran Madžarac wrote the paper and performed the literature search.

Željko Duić was involved in the case.

Josip Valetić was involved in the case.

Gordana Planinić-Radoš wrote the paper and performed the literature search.

All authors contributed to the editing of the paper.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

No funding was sought or secured in relation to this case report.

Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

References

[1] S. Mourad, J. Brown, C. Farquhar, Interventions for the prevention of OHSS in ART cycles: an overview of Cochrane reviews, Cochrane Database Syst. Rev. (1) (2017) https://doi.org/10.1002/14651858.CD012103.pub2 CD012103.

[2] M.M. Alper, L.P. Smith, E.S. Sills, Ovarian hyperstimulation syndrome: current views on pathophysiology, risk factors, prevention, and management, J Exp Clin Assist Reprod. 10 (2009) (6–3).

[3] M. van der Linden, K. Buckingham, C. Farquhar, J.A.M. Kremer, M. Metwally, Luteal phase support for assisted reproduction cycles, Cochrane Database Syst. Rev. (7) (2015) https://doi.org/10.1002/14651858.CD009154.pub3.

[4] Y. Yu, W. Xu, Z. Xie, Q. Huang, S. Li, Management and outcome of 25 heterotopic pregnancies in Zhejiang, China, Eur. J. Obstet. Gynecol. Reprod. Biol. 180 (2014) 157–161.

[5] R. Giurgis, I. Craft, Ectopic pregnancy resulting from gamete intrafallopian transfer and IVF. Role of ultrasonography in diagnosis and treatment, J. Reprod Med. 36 (1991) 793–796.

[6] Y.G. Kim, S.J. Lee, S.B. Han, M. Kim, Paralytic ileus after bilateral intravitreal injection of bevacizumab, Indian J. Ophthalmol. 64 (2016) 254–255.

[7] T. Felekis, C. Akrivis, P. Tsirkas, I. Korkontzelos, Heterotopic triplet pregnancy after in vitro fertilization with favorable outcome of the intrauterine twin pregnancy subsequent to surgical treatment of the tubal pregnancy, Case Rep. Obstet. Gynecol. (2014) 356131.

[8] J. Svare, P. Norup, S.G. Thomsen, P. Hornnes, S. Maigaard, P. Helm, K. Petersen, A.N. Andersen, Heterotopic pregnancies after in-vitro fertilization and embryo transfer - a Danish survey, Hum. Reprod. 8 (1993) 116–118.