

Case Report

Report of Two Cases of Pelvic Inflammatory Disease Complicating Transcervical Frozen Embryo Transfer

Marta Benito Vielba^{1,*}, Javier Navarro Sierra¹, Claudia Giménez Molina¹,
Marta Narváez Salazar¹, Ricardo Navarro Martín², María Pilar Conte Martín²

¹Department of Gynecology and Obstetrics, Hospital Miguel Servet, 50009 Zaragoza, Spain

²Department of Reproduction, Hospital Miguel Servet, 50009 Zaragoza, Spain

*Correspondence: martabv90@gmail.com (Marta Benito Vielba)

Academic Editor: Michael H. Dahan

Submitted: 31 October 2021 Revised: 8 December 2021 Accepted: 10 December 2021 Published: 16 January 2023

Abstract

Background: Pelvic inflammatory disease (PID) complicating transcervical embryo transfer, not related to previous oocyte aspiration, is an extremely rare event. However, it can lead to severe complications. **Case:** We report two cases of pelvic infection related to transcervical frozen embryo transfer. The case of one patient was complicated by a pelvic abscess, which required percutaneous drainage, and the case of the other patient was complicated by ascites, which was positive for chlamydia. **Conclusions:** Despite there not being enough evidence to recommend cervical cultures or antibiotic prophylaxis in all cases of embryo transfer, it would be advisable in those cases with a personal history of PID.

Keywords: pelvic inflammatory disease; frozen embryo transfer; oocyte aspiration; assisted reproductive techniques; pelvic infection

1. Introduction

Nowadays, embryo transfer in the context of *in vitro* fertilization (IVF) treatment is a procedure with a low incidence of complications [1].

Fresh embryo transfer has been the most common form of transfer in IVF cycles since the beginning of this technique. In recent years, improvements in vitrification protocols and an increase in preimplantation genetic testing of embryos have contributed to an increase in the number of frozen-thawed embryo transfer cycles. Consequently, the proportion of live births due to the success of this technique is increasing [2–4].

Initially, the main indication for this technique was to prevent ovarian hyperstimulation syndrome (OHSS). However, later studies have shown that controlled ovarian stimulation could lead to adverse effects in the endometrium, disrupting successful embryo-endometrium interaction. Therefore, it was suggested that performing frozen embryo transfer could improve the reproductive outcomes of IVF treatments [5,6].

In our center, embryo transfer is a standardized procedure. Firstly, we clean the cervix with saline solution, and cervical mucus is aspirated. Before inserting the catheter, the cervical canal is flushed with Vitrolife's G2 Plus medium. Then, a soft catheter (Labotect embryo transfer catheter, 190 mm) is loaded with embryos and handed to the clinician who inserts it through the cervical canal into the uterine cavity with abdominal ultrasound guidance. Finally, the embryos are placed 1–2 cm from the uterine fundus.

Reports regarding pelvic inflammatory disease (PID) after embryo transfer are extremely rare. Most of them are related to oocyte aspiration, where cervical and vaginal organisms could be inoculated during the procedure [7].

However, we report two cases of severe PID after frozen embryo transfer, which were not related to oocyte aspiration.

2. Case Report

2.1 Patient 1

The first patient was a 34-year-old Caucasian woman with a medical history of peritonitis after right ovarian cystectomy 17 years ago. The patient presented with sterility of 2 years evolution. The basic sterility study based on hormone analysis, seminogram, serology and ultrasound revealed the presence of a right hydrosalpinx (65 × 25 mm) in the initial ultrasound examination; however, this finding was not observed in subsequent ultrasounds. Besides, the seminogram revealed a very low sperm count and motility (REM 0.5 × 10⁶), so ICSI-IVF was performed. Embryo transfer was postponed for 4 months after ovarian stimulation and oocyte aspiration due to the high risk of suffering OHSS.

Two days after frozen embryo transfer, the patient developed a high fever (39 °C) and severe lower abdominal pain. Transvaginal ultrasonography revealed a pelvic mass in the right ovary (60 × 50 × 36 mm) with multiple cystic images. The white blood cell count was 14,200/mm³, and the C-reactive protein level was 16 mg/dL. She was hospitalized and received treatment with azithromycin and amox-



icillin clavulanic, low molecular weight heparin and analgesics. Endocervical culture was positive for *Escherichia coli*.

She was discharged 7 days after hospitalization due to clinical improvement. However, 11 days later, she came back to the emergency department due to recurrent abdominal pain and high fever. Her white blood cell count was 20,000/mm³, and the C-reactive protein level was 30 mg/dL. An abdominal Computed Tomography (CT) was performed, showing a right parauterine mass measuring 100 × 65 × 60 mm with cystic appearance with two septations and presence of thick walls. Besides, discrete edema of the adjacent fat and fluid sheet in the lesser pelvis were observed. All these findings were suggestive of tubo-ovarian abscess (Fig. 1).



Fig. 1. Right tubo-ovarian abscess.

Endocervical and vaginal cultures were positive for *Enterococcus faecalis*. The patient received intravenous antibiotic treatment with ceftriaxone, doxycycline and metronidazole without clinical improvement, so a percutaneous drainage of the abscess was performed by interventional radiology, obtaining a positive culture for *E. coli* infection. The antibiotic treatment was changed to piperacillin-tazobactam. The patient remained afebrile after abscess drainage. Several ultrasounds were performed during her admission to check the drainage and evolution of the abscess. She was discharged 8 days after drainage with a complete resolution of the abscess. Finally, she had a negative beta-hCG test after the resolution of the PID.

2.2 Patient 2

The second patient was a 28-year-old, secundigravid and Caucasian woman, with a history of hyperthyroidism treated with radioactive iodine and levothyroxine. Twelve years ago, she required laparoscopic drainage of a pelvic abscess due to PID. Since then, she had no history of pelvic infection, surgery or abdominal pain. She had undergone a voluntary interruption of pregnancy. The basic study of secondary sterility demonstrated no anomalies in both the patient and her husband. Neither vaginal nor endocervical

cultures were performed during the sterility study.

The patient came to the emergency department reporting intense abdominal pain and abdominal swelling for a month after having suffered a miscarriage at 6 weeks after a frozen embryo transfer performed at an external center. An emergency abdominal CT was performed, showing moderate ascites predominantly in the pelvic region (Fig. 2), which was initially treated with diuretics, albumin and anticoagulants.



Fig. 2. Moderate ascites in the pelvic region.

However, due to the poor clinical evolution of the patient, a culdocentesis guided by ultrasound was performed 4 days after her admission and 500 mL of peritoneal fluid was aspirated and analyzed, being positive for chlamydia. The endocervical culture was also positive for chlamydia. Antibiotic treatment with doxycycline was initiated, and the patient was discharged 2 days after culdocentesis with relevant clinical improvement.

3. Discussion

Pelvic infection after embryo transfer presenting as a pelvic abscess or ascites is an extremely rare event. Most cases are related to oocyte aspiration, where cervical and vaginal microorganisms could be inoculated into pelvic cavity [7,8].

Some authors propose the theory that oocyte aspiration could reactivate a latent infection in the fallopian tubes, as it has been described in other techniques, such as hysterosonography or hysterosalpingography [9,10].

However, pelvic infections not related to recent oocyte aspiration are not a frequent event. One of the cases in the literature reported an agonadal woman undergoing embryo donation, demonstrating that infection may result from transcervical embryo transfer, despite the precautions taken during the performance of this procedure [11]. Some reports have described cases with pelvic abscesses after transcervical frozen embryo transfer, which required laparoscopy for drainage [8,12].

Our cases illustrate the potential of embryo transfer to result in a severe pelvic infection. Both patients had a medical history of PID and peritonitis, so the reactivation of a latent infection could be the mechanism of the infection in these cases. The patient reported by Friedler *et al.* [12] also had history of PID.

Likewise, the placement of embryos into the uterine cavity using a catheter that passes through the cervix also entails the possibility of bacterial contamination during the embryo transfer procedure. In fact, there is growing evidence that bacterial contamination of the uterine cavity following transcervical embryo transfer can negatively affect the implantation rates and pregnancy outcomes [13–15]. Hamdoun *et al.* [16] observed that all patients with catheter contamination did not achieve pregnancy during embryo transfer. However, the pregnancy rate after IVF in patients with no catheter contamination was 61.2% in their study.

On the other hand, pelvic infections, such as chlamydia, mycoplasma, and ureaplasma, seem to be related to a longer period to achieve pregnancy and increased rates of pregnancy loss [17,18]. Bacterial vaginosis has also been considered an obstetrical and gynecological issue, and the link between bacterial vaginosis and preterm birth has been intensely studied. Likewise, some studies among infertile women have also suggested that bacterial vaginosis could negatively affect spontaneous female fecundity and IVF results [19].

This evidence makes us wonder if it would be necessary to recommend antibiotic prophylaxis in all patients before embryo transfer to prevent complications and to improve pregnancy rates.

Most of these studies conclude that standard aseptic measures, including sterile conditions during the procedure, help to minimize the risk of infection, but there is no evidence to recommend antibiotic prescription at the time of the embryo transfer, as it does not seem to improve pregnancy rates or to reduce complications [20,21].

In 2012, a Cochrane review evaluated the effectiveness and safety of antibiotic administration prior to embryo transfer during assisted reproductive technology cycles and concluded that administration of amoxicillin and clavulanic acid prior to embryo transfer reduced upper genital tract microbial contamination but did not alter clinical pregnancy rates, so this review does not recommend its general use [22]. Otherwise, antibiotic prophylaxis is recommended by some authors in patients with a recent history of pelvic infection [8].

Therefore, considering the rarity of this complication, nowadays, there is not enough evidence to recommend the routine performance of cervical cultures or antibiotic prophylaxis before embryo transfer. However, it could be considered in patients with a personal history of PID or risk factors for pelvic infections.

4. Conclusions

Frozen embryo transfer is a standardized procedure with a low rate of complications. PID after embryo transfer is an extremely rare event, but this complication could lead to pelvic abscesses or ascites, which can compromise the patient's health status. Despite its potential severity, nowadays, there is not enough evidence to recommend cervical cultures or antibiotic prophylaxis in all cases of embryo transfer. However, cervical cultures could be performed in those patients with risk factors or a personal history of PID in order to prevent complications and improve pregnancy rates.

Author Contributions

MBV—detailed data collection and careful writing of the manuscript. JNS—literature review and manuscript writing. CGM—literature review and manuscript writing. MNS—literature review and manuscript writing. RNM—clinical management and review of the scientific research. MPCM—clinical management and review of the scientific research.

Ethics Approval and Consent to Participate

An authorization from the Medical Records Department of our hospital was obtained to access and review the medical records of the women included in this study. Similarly, the authors obtained the approval of our local ethics committee. The number is C.P. - C.I. PI20/208. Informed consent was obtained from both patients included in this manuscript.

Acknowledgment

Thanks to all the peer reviewers for their opinions and suggestions which improved the quality of our manuscript.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Govaerts I, Devreker F, Delbaere A, Revelard P, Englert Y. Short-term medical complications of 1500 oocyte retrievals for *in vitro* fertilization and embryo transfer. *European Journal of Obstetrics & Gynecology Reproductive Biology*. 1998; 77: 239–243.
- [2] Pereira N, Rosenwaks Z. A fresh(er) perspective on frozen embryo transfers. *Fertility and Sterility*. 2016; 106: 257–258.
- [3] Doody KJ. Cryopreservation and delayed embryo transfer-assisted reproductive technology registry and reporting implications. *Fertility and Sterility*. 2014; 102: 27–31.
- [4] Pereira N, Petrini AC, Hancock KL, Rosenwaks Z. Fresh or Frozen Embryo Transfer in *In Vitro* Fertilization: an Update. *Clinical Obstetrics & Gynecology*. 2019; 62: 293–299.

- [5] Shapiro B, Daneshmand ST, Garner F, Aguirre M, Ross R. Contrasting patterns in *in vitro* fertilization pregnancy rates among fresh autologous, fresh oocyte donor, and cryopreserved cycles with the use of day 5 or day 6 stochastic may reflect differences in embryo-endometrium synchrony. *Fertility and Sterility*. 2008; 89: 20–26.
- [6] Roque M, Lattes K, Serra S, Solà I, Geber S, Carreras R, *et al.* Fresh embryo transfer versus frozen embryo transfer in *in vitro* fertilization cycles: a systematic review and meta-analysis. *Fertility and Sterility*. 2013; 99: 156–162.
- [7] Aragona C, Mohamed MA, Espinola MS, Linari A, Pecorini F, Micara G, *et al.* Clinical complications after transvaginal oocyte retrieval in 7098 IVF cycles. *Fertility and Sterility*. 2011; 95: 293–294.
- [8] Iliadis S, Gudmundsson J, Gambadauro P. Pelvic abscess following frozen embryo transfer. *Journal of Obstetrics and Gynaecology*. 2013; 33: 633–634.
- [9] Shavell VI, Le IP, Yelian FD. Tuboovarian Abscess after saline infusion sonohysterography: an unusual complication. *Journal of Minimally Invasive Gynecology*. 2009; 16: 652–654.
- [10] El-Toukhy T, Hanna L. Pelvic infection after oocyte retrieval: a preventable complication or an inevitable risk? *Journal of Obstetrics and Gynaecology*. 2007; 26: 701–703.
- [11] Sauer MV, Paulson RJ. Pelvic abscess complicating transcervical embryo transfer. *American Journal of Obstetrics and Gynecology*. 1992; 166: 148–149.
- [12] Friedler S, Ben-Shachar I, Abramov Y, Schenker JG, Lewin A. Ruptured tubo-ovarian abscess complicating transcervical cryopreserved embryo transfer. *Fertility and Sterility*. 1996; 65: 1065–1066.
- [13] Moore DE, Soules MR, Klein NA, Fujimoto VY, Agnew KJ, Eschenbach DA. Bacteria in the transfer catheter tip influence the live-birth rate after *in vitro* fertilization. *Fertility and Sterility*. 2000; 74: 1118–1124.
- [14] Fanchin R, Harmas A, Benaoudia F, Lundkvist U, Olivennes F, Frydman R. Microbial flora of the cervix assessed at the time of embryo transfer adversely affects *in vitro* fertilization outcome. *Fertility and Sterility*. 1998; 70: 866–870.
- [15] Egbase PE, Udo EE, Al-Sharhan M, Grudzinskas JG. Prophylactic antibiotics and endocervical microbial inoculation of the endometrium at embryo transfer. *Lancet*. 1999; 354: 651–652.
- [16] Hamdoun M, Braham M, Kacem K, Hannachi H, Zhioua F, Chakroun N, *et al.* Does bacterial colonization during embryo transfer have an impact on pregnancy rate in ICSI? : Tunisian preliminary results. *Journal of Gynecology Obstetrics and Human Reproduction*. 2021; 50: 101727.
- [17] Carbone L, Conforti A, LA Marca A, Cariati F, Vallone R, Raffone A, *et al.* The negative impact of most relevant infections on fertility and Assisted Reproduction Technology. *Minerva Obstetrics and Gynecology*. 2021. (in press)
- [18] Ahmadi A, Khodabandehloo M, Ramazanzadeh R, Farhadifar F, Roshani D, Ghaderi E, *et al.* The Relationship between Chlamydia trachomatis Genital Infection and Spontaneous Abortion. *Journal of Reproduction and Infertility*. 2016; 17: 110–116.
- [19] Haahr T, Jensen JS, Thomsen L, Duus L, Rygaard K, Humaidan P. Abnormal vaginal microbiota may be associated with poor reproductive outcomes: a prospective study in IVF patients. *Human Reproduction*. 2016; 31: 795–803.
- [20] Peikrishvili R, Evrard B, Pouly J, Janny L. Prophylactic antibiotic therapy (amoxicillin + clavulanic acid) before embryo transfer for IVF is useless. Results of a randomized study. *Journal De Gynecologie, Obstetrique Et Biologie De La Reproduction*. 2004; 33: 713–719. (In French)
- [21] Brook N, Khalaf Y, Coomarasamy A, Edgeworth J, Braude P. A randomized controlled trial of prophylactic antibiotics (co-amoxiclav) prior to embryo transfer. *Human Reproduction*. 2006; 21: 2911–2915.
- [22] Kroon B, Hart RJ, Wong BMS, Ford E, Yazdani A. Antibiotics prior to embryo transfer in ART. *Cochrane Database of Systematic Reviews*. 2012; CD008995.