Late Manifestation of Pelvic Abscess Following Oocyte Retrieval, for In Vitro Fertilization, in Patients with Severe Endometriosis and Ovarian Endometriomata

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Purpose: *Our purpose was to study the unusual and rare late manifestation of severe pelvic abscess, following oocyte pickup (OPU), for in vitro fertilization and embryo transfer (IVF-ET).*
Patients: *The patients were three infertile women with stage IV endometriosis and ovarian endometriomata, as the sole reason for their infertility. Medical and surgical modalities to treat endometriosis and infertility proved to be unsuccessful.*
Interventions: *All patients were prepared for IVF-ET employing a long GnRH-a and hMG protocol. Transvaginal OPU was performed under ultrasound guidance. Intravenous (iv) prophylactic antibiotic was routinely administered.*
Results: *All women underwent ET, and one conceived. Forty, 24, and 22 days after OPU, respectively, these patients presented with acute symptoms of severe pelvic inflammatory disease (PID) and were found to have pelvic abscess. Broad-spectrum iv antibiotics were employed in all cases, however, two patients did not respond and bilateral adnexectomy was eventually performed.*
Conclusions: *Severe endometriosis with ovarian endometriomata seems to be a significant risk factor for pelvic abscess development, following transvaginal OPU for IVF-ET. Prophylactic IV cefazolin does not seem to prevent this complication. Late manifestation of pelvic abscess supports the notion that the presence of old blood in an endometrioma provides a culture medium for bacteria to grow slowly after transvaginal inoculation.*

KEY WORDS: endometriosis; in vitro fertilization–embryo transfer; oocyte retrieval; ovarian endometriomata; pelvic abscess.

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INTRODUCTION

Throughout the last decade the transvaginal route for oocyte pickup (OPU) has gained wide acceptance. The safety and effectiveness of this technique have been documented and it is now considered to be the procedure of choice in women undergoing in vitro fertilization and embryo transfer (IVF-ET). Acute pelvic inflammatory disease (PID) following transvaginal OPU is an infrequent complication. The reported incidence of acute PID, within the first week after OPU, is 0.6% (1). However, the occurrence of late pelvic infection, specifically pelvic abscess, following transvaginal OPU, is rarely reported and its risk factors are still to be determined.

In the last few years we have encountered three cases of a pelvic abscess, following ultrasound-guided transvaginal OPU for IVF-ET. All three patients had severe endometriosis with ovarian endometriomata as the sole reason for their infertility and clinical manifestations of their PID first appeared more than 3 weeks after OPU. The pathogenesis of this rare occurrence is discussed, as well as the possible approaches to the management of endometriomata, during IVF-ET treatment.

CASE REPORTS

Patient 1. Patient 1 was a 34-year old gravida 0, with 12 years of primary infertility due to stage IV endometriosis (2) confirmed by laparoscopy. In addition she had bilateral tubal occlusion and dense pelvic adhesions. She did not conceive despite adhesiolysis, bilateral tuboplasty, and right endometriomatic cystectomy that was followed by danazol treatment. A second laparoscopy revealed bilateral endometriomata with

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severe pelvic adhesions, following which she had four unsuccessful attempts of IVF-ET. In the fifth attempt she was prepared by a long gonadotropin releasing hormone agonist (GnRH-a) (decapeptyl CR, 3.75 mg; Ferring, Malmo, Sweden) and human menopausal gonadotropin (hMG; Pergonal; Teva, Ramat-Gan, Israel) protocol. The serum estradiol (E_2)-level on the day of administration of human chorionic gonadotropin (hCG; Chorigon; Teva, Ramat-Gan, Israel) was 1450 pg/ml (conversion factor to SI units, 3.67). Twelve oocytes were retrieved and four embryos were transferred to the uterus (four were frozen), however, the patient did not conceive. A 4-cm endometrioma was intentionally aspirated from the left ovary on the day of OPU, but without much success. Only a slight amount of chocolate-like viscous material was removed and the endometriomata diameter and echogenicity did not change according to transvaginal scan (TVS). The patient received prophylactic antibiotics using intravenous (iv) cefazolin.

Forty days following the OPU the patient was admitted to the hospital due to a fever of 38.7°C, acute low abdominal pain, and a left palpable tender adnexal mass. The white blood cell count (WBC) was 13,900 and TVS revealed a normal uterus and right ovary, with a left multicystic 5.4 × 5.1-cm mass with hyperechogenic echoes. Laparoscopy was not informative due to dense adhesions of endometriosis. At laparotomy, puncture of the left ovary revealed 30 ml of bad-smelling chocolate-like material. The appendix was covered with patches of endometriosis and was removed. Broad-spectrum iv antibiotics were commenced, employing ampicillin, gentamicin, and metronidazole, followed by gradual clinical improvement. The cultured chocolate material was sterile. The patient was discharged home with oral amoxycillin and metronidazole in addition to im decapeptyl CR therapy.

Eight weeks later the patient was readmitted to hospital with a 39°C fever, low abdominal pain, and signs of pelvic peritonitis. The WBC was 16,600, the erythrocyte sedimentation rate (ESR) was 95 and 125 mm in the first and second hours, respectively, and TVS revealed bilateral 5 × 5-cm complex adnexal masses compatible with bilateral tuboovarian abscesses. Intravenous ampicillin, gentamicin, and metronidazole were initiated. Despite some clinical improvement, the sonographic findings did not change. Three weeks after her second admission the patient had bilateral salpingo-oophorectomy. During the operation, spillage of pus was noticed from both adnexa. The postoperative course was uneventful and the patient was discharged home with oral cefuroxime treatment.

Patient 2. Patient 2 was a 36-year-old gravida 0, with 10 years of primary infertility due to stage IV endometriosis with bilateral 5 × 6-cm endometriomata. Danazol treatment was initiated, however, a second laparoscopy did not show any improvement. Four previous attempts of IVF-ET were unsuccessful. Her fifth attempt was prepared by the long GnRH-a and hMG protocol. The maximal serum E_2 level on hCG day was 4242 pg/ml (conversion factor to SI units, 3.67). Ten oocytes were retrieved and three were fertilized and transferred to the uterus, but the patient did not conceive. The OPU was performed transvaginally under TVS guidance and iv cefazolin prophylaxis.

Twenty-four days later the patient was admitted to hospital due to a 38.5°C fever and dry cough. Her physical examination was unremarkable except for two enlarged, nontender ovaries, thought to be the result of ovarian hyperstimulation. Her WBC was 19,100 and her ESR 120/138 mm. She was admitted to the internal medicine department and a thorough investigation for fever of unknown origin was performed. With a suspicion of Q fever, she was treated initially with oral tetracycline and thereafter by ofloxacin, with gradual improvement and a drop of fever to normal

Four weeks after discharge the patient was readmitted with a 39.6°C fever, low abdominal pain, and bilateral very tender adnexal masses. The WBC was 22,700 and TVS revealed bilateral multicystic and complex adnexal masses, the right 9.0 × 5.5 and the left 8.0 × 4.5 cm, compatible with tuboovarian abscesses. Broad-spectrum iv antibiotics were initiated, employing ampicillin, gentamicin, and clindamycin, with no clinical improvement. A laparotomy was therfore indicated and bilateral salpingo-oophorectomy was performed. The postoperative course was uneventful. At present, 2 years after the operation, she is healthy and in anticipation of oocyte donation.

Patient 3. Patient 3 was a 29-year-old gravida 1, para 0, with 4.5 years of infertility due to diffuse pelvic endometriosis with bilateral endometriomata. She had operative laparoscopy with bilateral endometriomatic cystectomies followed by GnRH-a therapy. After down regulation, hMG was initiated for IVF-ET treatment. The serum E_2 level on hCG day administration was 2241 pg/ml (conversion factor to SI units, 3.67). Three oocytes were retrieved, and two fertilized and transferred to the uterus. Oocyte pickup was performed transvaginally using ultrasound guidance and iv cefazolin prophylaxis. Both ovaries still had a few small endometriomata (1–1.5 cm in diameter) on the day of OPU.

Twenty-two days following OPU, the patient was admitted to the hospital due to 38 9°C fever, nausea, low abdominal pain, and bilateral tender adnexal masses. Transvaginal scan revealed bilateral 4 × 6-cm complex adnexal masses, compatible with tuboovarian abscesses. Her WBC was 21,000 and her ESR 124/145 mm. Blood, urine, and cervical cultures were negative. The serum β-hCG level was 283 mIU/ml. Intravenous ampicillin, gentamicin, and clindamycin were initiated. Under this regimen, a marked clinical improvement was noticed, however, a fever of up to 38°C was still documented in the evenings. On the sixth day of admission, ampicillin and gentamicin were stopped and ceftriaxone treatment was commenced. Under the new regimen, the fever dropped to normal and the WBC to 11,000. After 15 days of iv antibiotic therapy, the patient was discharged home with oral cefuroxime and clindamycin. On discharge, TVS showed a single intrauterine viable fetus. Ultrasound follow-up showed a gradual improvement and shrinkage of the adnexal masses. At 14 weeks of gestation TVS demonstrated a viable normal fetus and normal ovaries except for a right simple 2.9 × 2.1-cm ovarian cyst. The pregnancy progressed uneventfully thereafter, and the woman delivered a normal female newborn, at term, weighing 2850 g.

DISCUSSION

In this report we have presented three unusual cases with a pelvic abscess that had developed more than 3 weeks following transvaginal OPU for IVF-ET. In all three women, tuboovarian abscesses developed similarly in endometriomatic ovaries, in patients who had stage IV endometriosis as the sole reason for their infertility. The late manifestation of the pelvic abscess, in all cases, supports the notion that the presence of old blood in an endometrioma provides a culture medium for bacteria to grow slowly after transvaginal inoculation.

Although a thorough vaginal lavage is routinely performed before OPU, complete sterilization of the vagina is never achieved. Minimal inoculation of the ovarian follicles in "healthy" ovaries is usually overcome without clinical symptoms, possibly due to antibiotic prophylaxis (3). In endometriomatic ovaries, the pseudocapsule of the endometriomata and the old blood within may both prevent antibiotic prophylaxis from overcoming the transvaginal bacterial inoculation. Therefore, endometriomatic aspiration during OPU, as was intentionally performed in case 1, should be avoided.

Previous reports have shown that ovarian endometriomata aspiration is feasible under TVS guidance and is a low-risk procedure (4). These findings are not consistent with the pelvic abscess formation presented in this report. It may be speculated that the supraphysiolgical E_2 levels, achieved after superovulation with hMG, stimulate ectopic tissue of endometriosis and neovascularization in the endometriomatic wall. This may be an additional risk factor for infection following transvaginal endometriomata aspiration during OPU.

Other explanations for the late pelvic infection could have been reactivation of a latent pelvic infection or initiation of a new infection following trauma to a loop of large bowel during the OPU. Although these assumed routes of infection could not be completely refuted, they appear to be unlikely. It is our belief that these other etiologies would have clinically manifested themselves much earlier.

There are several reasons to treat ovarian endometriomata before superovulation for IVF-ET. A definite diagnosis could usually be achieved after aspiration, and in some cases, it can serve as the conclusive treatment for pelvic pain. In addition, aspiration of the endometriomata can improve the accessibility of follicles during the OPU. Moreover, it has been shown that ovarian endometriomata may reduce folliculogenesis and that its aspiration before superovulation could improve the oocyte quality and clinical pregnancy rate (5). Nevertheless, considerable confusion and disagreement still remains regarding the appropriate treatment of ovarian endometriomata and the effectiveness of each of the medical, surgical, or combined approaches of treatment is still in debate (6).

To the best of our knowledge, no pelvic abscess formation has been reported following transabdominal OPU using either ultrasound guidance or the laparoscopic approach. This could imply another indirect evidence for the transvaginal ovarian inoculation theory for pelvic abscess development. It is therefore suggested that in patients with ovarian endometriomata, transabdominal OPU under ultrasound guidance should be considered in order to reduce the risk of late infection.

In conclusion, ovarian endometriomata in patients with severe endometriosis seems to be a significant risk factor for late pelvic abscess formation following

transvaginal OPU for IVF-ET. Moreover, it is suspected that abscess formation is the result of endometriomata inoculation by vaginal bacteria. Single-dose antibiotic prophylaxis by cefazoline does not seem to prevent this late complication. A broader-spectrum and/or a more prolonged antibiotic prophylaxis should be considered in these cases. Thorough vaginal preparation and avoidance of repeat penetration of the vaginal wall are specifically important in these patients. Moreover, endometriomata aspiration during OPU is unequivocally discouraged. Close follow-up for signs of late pelvic infection is of utmost importance. Prior treatment of endometriomata before superovulation by aspiration or by operative laparoscopy is to be considered. Finally, transabdominal OPU under ultrasound guidance should be taken into account when planning for IVF-ET in patients with multiple ovarian endometriomata.

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