

## Endometriosis May Contribute to Oocyte Retrieval-Induced Pelvic Inflammatory Disease: Report of Eight Cases

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Pelvic inflammatory disease (PID) is a rare complication of transvaginal oocyte retrieval. It may result in failure of assisted reproductive techniques (ART). During a 7 years period, 5958 transvaginal ultrasound-guided oocyte retrievals resulted in 10 cases of acute PID. Eight out of 10 patients were diagnosed infertile because of endometriosis. Two patients had mild ovarian, 3 had stage III, and 2 had stage IV endometriosis. One patient had a 3-4 cm ovarian endometrioma. After treatment, no mortality was encountered among the 10 patients, although none of them conceived. This observation supports the previous reports that endometriosis can raise the risk of PID after oocyte retrieval. More vigorous antibiotic prophylaxis and better vaginal preparation are recommended when oocyte pickup is performed in patients with endometriosis.

**Keywords:** Endometriosis, Oocyte Retrieval, Pelvic Inflammatory Disease

### Introduction

ART is currently considered a potential solution for cases with infertility problems. Transvaginal oocyte retrieval in ART is a routine procedure and is documented to be safe and effective. However, it is sometimes associated with complications including puncture of blood vessels, perforation of the bowel, bleeding from the vagina vault puncture and pelvic infection (Ashkenazi *et al.*, 1994; Everse *et al.*, 1998). PID and subsequent pelvic abscess formation are rare complications of oocyte retrieval, which usually result in failure of the procedure. It is reported to occur in 0.2-0.5 % of transvaginal oocyte retrievals (Ashkenazi *et al.*, 1994; Govaerts *et al.*, 1998).

Endometriosis is found in 25-40% of female infertility, as compared to 2-5% of the general population (Hickman, 2002). In vitro fertilization-embryo transfer (IVF-ET) is now a recognized treatment for refractory endometriosis associated infertility. On the other hand, endometriosis is proposed to be a risk factor for pelvic inflammation and abscess development following transvaginal ovum pickup (Younis, *et al.*, 1997; Den Boon *et al.*, 1999).

The presence of old blood in endometrioma is suggested to provide a culture medium for bacteria to grow slowly after transvaginal inoculation which may

explain the role of endometriosis in predisposing the patients with PID (Younis, *et al.*, 1997).

This communication represents our seven years of experience with oocyte retrieval-induced acute PID. We present ten cases of PID following oocyte retrieval, eight of them with endometriosis.

### Patients

From 1994 to 2000, a total of 5958 cycles of IVF or ICSI were performed at our institute. Following pretreatment with clomiphene citrate, GnRH, and hMG protocols, patients underwent vaginal ultrasound-guided oocyte pickup. The vagina was irrigated with sterile saline solution. Patients routinely received doxycycline (100 mg BID) from the day of oocyte retrieval till the day of ET (2-3 days) as prophylactic antibiotic therapy. Out of 5,958 cycles, 10 cases were diagnosed and treated as oocyte retrieval-induced PID (0.12 %). Diagnosis of PID was based on the signs of peritonitis on physical examination, cervical and adnexal tenderness, rise of body temperature to  $>37.8^{\circ}\text{C}$  for 48 h, cervical discharge, leukocyte count above 12,000 and elevated erythrocytic sedimentation rate. The PID was usually diagnosed 4-7 days after the procedure.

All PID patients were diagnosed with female factor infertility, among them 8 were diagnosed with

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endometriosis. The diagnosis of endometriosis was based on laparoscopic findings plus pelvic pain, infertility and dysmenorrhea (Muse and Wilson 1991). The diagnosis was confirmed by histological examination. Two patients had mild ovarian, 3 had stage III, and 2 had stage IV endometriosis. One patient had a 3-4 cm ovarian endometrioma. The two patients lacking endometriosis were a 38 years old female with history of bilateral tubal obstruction and a 21 years old female with previous history of PID with a diagnosis of pre-tubal adhesion.

Out of ten patients with PID, five were successfully treated medically, three of them received intravenous clindamycin + gentamycin and the other two received a third antibiotic (ampicillin). The other patients did not respond to medical treatment and underwent needed surgical interventions. In one case transvaginal drainage of abscess was performed. Two patients underwent laparoscopic drainage of abscess and two patients needed laparotomy, one of them had a large tubo-ovarian abscess not appropriate for laparoscopic drainage. No mortality was encountered, although none of the patients were conceived.

## Discussion

PID is known as a rare complication of ovum pickup in ART program. This paper reports 10 cases of PID following oocyte pickup with the suggestion of endometriosis as a potential risk factor. Inoculation of vaginal bacteria and anaerobe opportunists is suggested to be the cause of PID following oocyte retrieval (Bennett *et al.*, 1993). Microorganisms of vagina are suggested to be the etiological pathogens in pelvic abscesses when transvaginal oocyte retrieval is used (Bennett *et al.*, 1993). However, no pelvic infection has so far been reported with laparoscopic or abdominal oocyte retrievals (Bennett *et al.*, 1993). Vaginal preparation has been made by different methods including the use of saline or povidone-iodine. Although, we have routinely irrigated the vagina with saline solution, no differences in the incidence of PID were noticed between our results and those of others. In two reports by Meldrum (1998) and Evers *et al.* (1998), no cases of PID in small group of patients were diagnosed. The former study used intravenous cefazolin and vaginal irrigation with povidone-iodine, and the latter using only 10% povidone-iodine. Larger series report rare cases of serious infections using sterile saline (2 out of 400) (Borlum and Maigaard 1989) and Earle's balanced salt solution (6 out of 1500) (Govaerts *et al.*, 1998). Although, prophylactic antibiotic therapy is still a very important issue, there are some concerns about it. The vigorous use of antibiotics, although useful in some cases, may lead to antibiotic resistance.

A finding of our study, which is similar to other reports, is the total failure of pregnancy in the presence of PID. The same observations have been reported previously by other investigators (Ashkenazi *et al.*, 1994; Govaerts *et al.*, 1998). Several possible explanations for the role of infection in reducing pregnancy success have been suggested. Introducing endotoxin releasing bacteria into the peritoneal cavity during transvaginal oocyte retrieval may induce abortion by promoting the release of prostaglandins as well as various autocoids, catecholamines and cortisol which play some role in the termination of pregnancy. Moreover, local inflammatory reaction and fever may also affect the success rate of pregnancy (Orvieto and Ben-Rafael 1999).

There have been some case reports on the coexistence of endometriosis (Younis *et al.*, 1997; Padilla 1993) or its history (Den Boon *et al.*, 1999) in patients with PID following ART treatment. Younis *et al.* (1997) presented three cases of severe pelvic abscess following oocyte pickup for IVF-ET in whom stage IV endometriosis or ovarian endometrioma were previously diagnosed as the sole reason for infertility. In contrast, Ashkenazi *et al.* (1994) failed to show a higher incidence of endometriosis among their patients: 2 cases of endometriosis in 28 PID patients among 4771 ovum pick-ups. It has been suggested that both the pseudocapsule of endometrioma and its inside old blood may prevent antibiotic prophylaxis from overcoming the transvaginal bacterial inoculation (Younis *et al.*, 1997). A case reported revealing right tubo-ovarian abscess (TOA) after transvaginal ultrasound-guided aspiration of an ovarian endometrioma before IVF-ET led to the exploratory laparotomy ensured and right salpingo-oophorectomy was performed (Wei and Chen, 1998). In other cases of endometriosis, small pools of old blood may act as culture media for the inoculated bacteria. Deposit of TOA is an uncommon complication in pregnant women, that leading serious complication such as surgery, ICU admission and preterm delivery only one subject developed a TOA during pregnancy following IVF-ET in this report.

Predisposing factors for TOA are previous laparotomy, structural genital anomalies, endometriosis and hydrosalpinx during ART and pregnancy (Matsunga *et al.*, 2003). In addition, due to the adverse effect of endometriomas on IVF outcome, it is suggested that endometrioma should be removed in patients with endometriosis prior to IVF admission. Preconception evaluation and treatment should be considered for such condition (Matsunga *et al.*, 2003).

In conclusion, endometriosis may be a predisposing factor for oocyte retrieval-induced PID. In regards to the few investigations available, it is rather soon to conclude a management protocols. However, some precautions may be useful for cases with endometriosis

that undergo oocyte retrieval. Vaginal preparation with better bactericidal substances as well as stronger antibiotic prophylaxis might be useful in the prevention of PID. In addition, full evaluation and removal of endometrioma should be considered for the patients undergoing IVF (Matsunga *et al.*, 2003). However, non-vaginal methods of oocyte recovery like transabdominal approach in cases with endometriosis and pelvic adhesion seem preferable.

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