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## Case report

# Two patients with endometriosis require peripregnancy surgical treatment for pelvic abscesses after egg collection and embryo transfer

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#### ABSTRACT

Assisted reproductive technology procedures infrequently cause pelvic abscesses, but the risk is higher in patients with endometriosis. If antibiotic treatment of a pelvic abscess is unsuccessful, surgery is required—even during pregnancy. We report two patients with endometriosis who suffered from pelvic abscesses formed after egg collection and embryo transfer. Patient 1 underwent laparoscopic resection of the left adnexa and right ovarian cystectomy after diagnosis of the implantation failure. Surgical findings showed severe adhesions in the pelvis due to endometriosis. Patient 2 underwent open drainage surgery at 11 weeks of pregnancy due to panperitonitis caused by a pelvic abscess. The patient delivered at 36 weeks of gestation. We conclude that egg collection and embryo transfer in patients with endometriosis confers a high risk for pelvic infection. An accurate diagnosis and appropriate treatment, including surgery, are mandatory in case of severe pelvic abscesses during pregnancy to save both mother and fetus.

## Introduction

Pelvic and peritoneal abscesses are rare complications of pregnancy [1] because there are protective mechanisms from ascending infection to the uterus during pregnancy, conferred by the cervical mucus plug and intact amniotic membranes. However, patients with endometriosis who undergo egg collection (EC) and embryo transfer (ET) as part of assisted reproductive technology (ART) are at an increased risk of pelvic infection. [2] Consequently, pelvic infections in this patient population may necessitate therapeutic intervention during early pregnancy.

Managing pelvic peritonitis during early pregnancy is complicated by the need to minimize radiation exposure from imaging like computed tomography (CT). Additionally, physiological changes during pregnancy can affect the interpretation of blood test results. The fetus may be particularly vulnerable during organogenesis or before complete placental development, with varying sensitivities to teratogens depending on the gestational age. Furthermore, the effects of general anesthesia and surgical procedures on the developing fetus during organogenesis remain largely unknown.

While there is no universally accepted management protocol, surgical drainage or conservative surgical procedures combined with antibiotic therapy are generally recommended for pelvic abscesses

during pregnancy, especially if there is no clinical improvement with antibiotics alone or in the presence of complications. [3,4] This approach aims to resolve the infection while minimizing risk to both mother and fetus. Uncontrolled pelvic infections are associated with a higher risk of pregnancy loss. [5] Therefore, careful monitoring of high-risk patients and individualized treatment plans based on gestational age are crucial. We present two cases of patients with endometriosis who developed pelvic abscesses after EC and ET, necessitating surgical intervention during the peripartum period. Patient 1 underwent surgery immediately following a spontaneous abortion, while Patient 2 required surgery during the first trimester. Neither patient responded adequately to conservative management. Both patients gave written consent to publish their information as a case report.

## Case. Presentations

## Patient 1

A woman in her mid-30s with a history of cesarean sections presented to a fertility clinic seeking to conceive through ART. She reported a regular 28-day menstrual cycle with severe dysmenorrhea and had been diagnosed with bilateral ovarian endometriomas. The patient

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opted to proceed with further ART, undergoing EC followed by frozen ET two months later at the same clinic. The day following the ET procedure, she developed a high fever and lower abdominal pain, prompting referral to another hospital. Her symptoms and inflammatory markers improved after two weeks of intravenous carbapenem antibiotic therapy (meropenem 3 g/day). However, transvaginal ultrasonography and pelvic MRI revealed a 5-cm abscess in the left ovary, leading to her referral to our hospital for further management.

Initial vital signs were stable: blood pressure (BP) 121/68 mmHg, heart rate (HR) 100 bpm, and body temperature  $36.6^{\circ}$ C. Laboratory results indicated relatively mild inflammation with a white blood cell count (WBC) of  $5600/\mu$ L (Reference Range:  $4500-10000/\mu$ L) and a Creactive protein (CRP) level of 0.06 mg/dL (Reference Range: less than 1.0 mg/dL), but her carbohydrate antigen 125 (CA-125) was elevated at 179.7 U/mL (Reference Range: 0-35 U/mL). A negative pregnancy test 14 days post-ET confirmed implantation failure. Ultrasound and CT imaging revealed a 4-cm cystic lesion within the left ovary, and pelvic MRI demonstrated a thick-walled cyst, highly suggestive of abscess formation (Fig. 1A). Considering her strong desire for future fertility, we recommended laparoscopic resection of the left adnexa as the primary treatment.

During surgery, dense intestinal adhesions were noted on the posterior aspect of the uterus, initially obscuring both the ovary and fallopian tube. Upon adhesiolysis, yellowish-white purulent material was observed draining from the left ovary (Fig. 1B), and chocolate-colored fluid consistent with an endometrioma was seen emanating from the right ovary (Fig. 1C). The left adnexa was resected, the right ovarian cyst was removed, and the pouch of Douglas was opened. The operative time was approximately 2.5 hours with minimal intraoperative blood loss.

The revised American Society for Reproductive Medicine (rASRM) classification of endometriosis score was 154, indicating stage IV disease. Postoperative laboratory values showed a WBC of  $9000/\mu L$  and CRP of 1.91 mg/dL on postoperative day 1, and  $6000/\mu L$  and 4.29 mg/dL on day 3, respectively. Pathology confirmed an endometriotic cyst of the left adnexa and a right ovarian endometrioma. Intraoperative cultures from the left ovarian abscess were negative. The patient had an uneventful postoperative course and was discharged on the fourth postoperative day. She is considering repeating frozen ET in the near future.

#### Patient 2

A woman in her mid-30s with a history of one prior spontaneous vaginal delivery presented to a fertility clinic for ART. She reported a regular 28-day menstrual cycle with dysmenorrhea. Her surgical history was notable for an appendectomy and prior removal of a left ovarian endometrioma. Following EC and fresh ET, the patient conceived. At nine weeks gestation, she presented to the hospital with lower abdominal pain. Laboratory studies revealed elevated inflammatory markers, and she had been treated with intravenous cephalosporin antibiotics (cefazolin 2 g/day) for presumed pelvic inflammatory disease. Cefazolin was chosen for this patient because she was pregnant and there was concern about the potential teratogenic effects of later-generation cephalosporins. However, her inflammatory markers remained elevated, and her abdominal pain worsened, with the development of rebound tenderness. At ten weeks gestation, the patient was referred to our department for further management.

Bimanual examination revealed marked uterine and adnexal

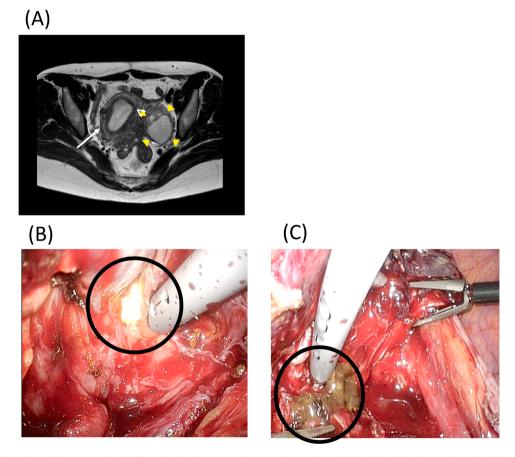


Fig. 1. Preoperative imaging and intraoperative findings during laparoscopic surgery in patient 1;(A) Axial pelvic T2W MR imaging shows a thickened capsule around cysts in the left ovary; the contents are suspicious of the abscess. An arrow indicates the uterus, and a triangle characterizes the left ovarian cyst. (B) Yellowish-white fluid flows from the left ovary. A black circle indicates the rupture point of the cyst. (C) Chocolate-like fluid is flowing from the right ovary. A black circle indicates the rupture point of the cyst.

tenderness. Vital signs showed a temperature of 37.3°C, BP of 111/ 71 mmHg, and HR of 78 bpm. Laboratory studies demonstrated a significantly elevated WBC of 21400/µL and a CRP of 12.77 mg/dL. Blood cultures obtained earlier during the admission were negative. Ultrasound revealed bilateral ovarian cysts, 4 cm on the right and 5 cm on the left. A viable intrauterine pregnancy with normal fetal cardiac activity at 11 weeks gestation was confirmed (Fig. 2A). Pelvic MRI demonstrated a thick-walled cystic structure in the pouch of Douglas, concerning for an abscess (Fig. 2B). Given these findings, a diagnosis of pelvic peritonitis secondary to a pelvic abscess was made, and a laparotomy was planned. Intraoperatively, the pouch of Douglas was found to be obliterated by dense adhesions to the sigmoid colon and adnexa. Upon adhesiolysis, a yellowish-white purulent collection was identified within the pouch of Douglas (Fig. 2C). Both ovaries were enlarged, measuring approximately 4 cm, but contained only serous fluid without evidence of infection. No distinct cyst wall was identified. The operative time was approximately 1.5 hours, with an estimated blood loss of 100 mL. Intraoperative cultures from the pelvic abscess grew Peptostreptococcus species. The patient's postoperative course was uneventful. Her WBC count and CRP level were 12400/µL and 15.79 mg/dL on postoperative day 1, respectively, improving to 6500/µL and 4.38 mg/ dL on postoperative day 4. She was followed closely in our outpatient department throughout her pregnancy and underwent a spontaneous vaginal delivery at 36 weeks of gestation. The neonate was a male infant weighing 2424 g with Apgar scores of 10 and 10 at 1 and 5 minutes, respectively.

#### Discussion

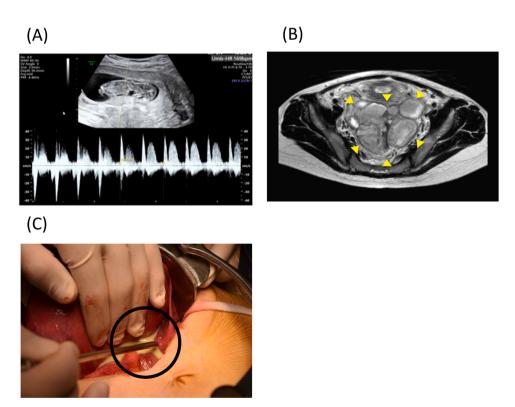
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The optimal management of endometriosis before ART remains controversial. While Benaglia et al. reported no cases of pelvic abscess in a series of 214 IVF cycles performed in women with endometriomas, suggesting a low risk (0.0; 95 % CI 0.0–1.7 %),[6] the increasing number of patients undergoing ART for endometriosis-associated infertility,

as highlighted in our report, warrants further consideration of this issue. In Japan, the average age of marriage has been increasing, reaching 31.0 years for husbands and 29.4 years for wives in 2020 (Statistical Handbook Japan. 2021). This trend towards delayed childbearing has contributed to a rapid increase in the number of patients undergoing ART procedures. Furthermore, with an estimated prevalence of 25–50 % in women with infertility,[7] endometriosis is increasingly encountered in the ART setting. Our prior work has demonstrated that transvaginal procedures commonly used in ART, such as EC and ET, pose a risk of infection in patients with endometriosis.[8] Vaginal-cervical microbial contamination during ET is not only associated with significantly decreased pregnancy rates but can also lead to pelvic abscess formation, including tubo-ovarian abscesses, with a reported incidence of 0.2–0.3 %.[9]

Pelvic abscesses typically present with fever, lower abdominal pain, and signs of peritoneal irritation.[10] However, diagnosing pelvic inflammatory disease during pregnancy is challenging due to the physiological changes that can mask or mimic these symptoms.[11] Furthermore, imaging modalities such as CT and MRI are often limited during pregnancy, particularly during fetal organogenesis. Due to overlapping symptoms, pelvic inflammatory disease in pregnancy is frequently misdiagnosed as appendicitis or acute pyelonephritis, especially in the presence of high fever, persistent right-sided abdominal pain, abdominal tenderness, and leukocytosis.[12]

The choice of antibiotics for each patient was based on their individual clinical presentation and the suspected source of infection. Patient 1 presented with a high fever and lower abdominal pain, and her imaging suggested a left ovarian abscess. Meropenem, a broad-spectrum carbapenem antibiotic, was chosen for its activity against a wide range of bacteria, including those commonly associated with pelvic infections. Patient 2 presented with lower abdominal pain and rebound tenderness, and her imaging suggested a pelvic abscess. Cefazolin, a first-generation cephalosporin antibiotic, was chosen for its activity against grampositive bacteria, which are commonly associated with pelvic



**Fig. 2.** Preoperative imaging and intraoperative findings during laparotomy in patient 2; (A) An 11-week fetus with normal cardiac activity in the uterus; (B) Axial pelvic T2W MR imaging shows a cystic lesion in the rectouterine pouch, resembling a ductal structure with a thick membrane. The area considered a triangle surrounds an abscess. (C) As the adhesions in the rectouterine fossa are peeled away, yellowish-white drainage is visible (indicated by a black circle).

inflammatory disease.

In our second case, *Peptostreptococcus* spp. was identified in the pelvic abscess. This Gram-positive anaerobic coccus is a common inhabitant of the skin, gastrointestinal tract, and female genital tract and is recognized as a significant pathogen in pelvic abscesses.[13] It is also frequently implicated in various other infections, including skin abscesses, diabetic foot ulcers, pressure ulcers, wound infections, and bacterial vaginosis. Although both patients had received antibiotics prior to our evaluation, making it difficult to exclude other potential causative organisms, initial empiric broad-spectrum antibiotic therapy covering enteric and anaerobic bacteria is crucial in the management of pelvic abscesses.

Several pathogenic mechanisms have been proposed for pelvic abscess formation during pregnancy. Risk factors include a history of pelvic inflammatory disease, previous laparotomy, and structural genital tract abnormalities.[11] Common causative organisms include enteric and anaerobic bacteria, such as *Escherichia coli*, *Streptococcus* spp., and *Klebsiella pneumoniae*.[14] Potential mechanisms include inoculation of the uterus and adnexa with vaginal flora, reactivation of a latent pelvic infection, or direct intestinal injury. Furthermore, pelvic infections tend to be more severe in patients with endometriosis. These infections may necessitate surgical intervention if conservative management fails.

Abscesses larger than 5 cm in diameter are often refractory to antibiotic therapy alone, [15] and surgical intervention or drainage should be considered if there is no clinical improvement within 48–72 hours of initiating antibiotics. [16] While surgical management of tubo-ovarian abscesses has been reported during pregnancy, [5] [11] it carries a potential risk of pregnancy loss, especially in the first trimester. Therefore, a conservative approach with antibiotics and potentially drainage should be considered during early pregnancy.

In conclusion, we present two cases of patients with complicated endometriosis who underwent ART and subsequently developed pelvic abscesses during pregnancy, ultimately requiring surgical intervention. These cases highlight the increased risk of pelvic infection associated with EC and ET in patients with endometriosis. Given the challenges in managing severe pelvic abscesses during pregnancy, meticulous monitoring of high-risk patients is essential. Timely and accurate diagnosis, along with appropriate treatment, including surgical intervention when indicated, are crucial to optimize maternal and fetal outcomes. Progression to sepsis significantly worsens the prognosis for the pregnancy. In cases of persistent abscess despite conservative management or when there is a concern for immediate maternal or fetal well-being, surgical intervention should be strongly considered. The optimal timing of surgery should be determined on a case-by-case basis, taking into account gestational age, abscess characteristics, and the patient's overall clinical status

Ethical approval:

This study did not involve patients or volunteers

## **Authors' Contributions**

All authors have contributed sufficiently in this work to warrant authorship and take public responsibility for it. TS, MT and MI managed the patients and collected the data. MT drafted the manuscript. SA supervised the manuscript.

#### Consent

Written informed consents were obtained from the patients for the publication of this case report and accompanying images.

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## CRediT authorship contribution statement

Ichikawa Masao: Investigation. Toyoshima Masafumi: Writing – original draft, Investigation, Data curation, Conceptualization. Shiraishi Tatsunori: Investigation. Akira Shigeo: Investigation.

## **Declaration of Competing Interest**

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Masafumi Toyoshima reports financial support was provided by Nippon Medical School Hospital. Tatsunori Shiraishi reports financial support was provided by Nippon Medical School Hospital. Masao Ichikawa reports financial support was provided by Nippon Medical School Hospital. Shigeo Akira reports financial support was provided by Meirikai Tokyo Yamato Hospital. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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