

Ectopic pregnancy following intracytoplasmic sperm injection-embryo transfer (ICSI-ET)

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Abstract

Ectopic pregnancy (EP) is defined as a pregnancy implanted outside of the endometrial cavity and one of the leading causes of maternal morbidity and mortality during the first trimester. There are several risk factors of ectopic pregnancy have been described especially following ART. However, prevalence of ectopic pregnancy is varied and slightly higher in pregnancies following ART. Several mechanisms have been described of EP following ART. Serial serum beta hCG and pelvic sonographic screening facilitates early diagnosis and avoid the delay to initiate treatment for EP in ART patients. No particular treatment modality is shown to be superior in EP.

In this case, we reported two cases of ectopic tubal pregnancy following Intracytoplasmic Sperm Injection (ICSI)-Embryo Transfer (ET) which were successfully managed without complications by laparoscopic salpingectomy

our own practice we present a management approach for future pregnancies with particular focus on fetal surveillance.

Key words: ectopic pregnancy, intracytoplasmic sperm injection (ICSI), laparoscopic salpingectomy

Introduction

Ectopic pregnancy (EP) is defined as a pregnancy implanted outside of the endometrial cavity, such as a fallopian tube, cervix, caesarean scar, interstitial part and abdominal cavity. The incidence of ectopic pregnancy is 1.5-2% after spontaneous pregnancy and ectopic pregnancy can occur following Assisted Reproductive Technology (ART), though this is uncommon¹. The incidence of ectopic pregnancy after IVF is 2-5%, and majority are tubal². Ectopic pregnancy is one of the leading causes of maternal morbidity and mortality during the first trimester.

Delayed diagnosis or misdiagnosis may lead to such complications as severe intraabdominal bleeding and subsequent hypovolemic shock associated with maternal morbidity and mortality. Early diagnosis and timely intervention facilitate optimal outcome of ectopic pregnancy.

In this article, we report two cases of ectopic tubal pregnancy following Intracytoplasmic Sperm Injection (ICSI)-Embryo Transfer (ET) which were successfully managed without complications by laparoscopic salpingectomy.

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Case 1

38 years old women with a history of subfertility for eight years self-referred to ART treatment after unsuccessful basic subfertility treatment. She did not have a significant past medical history but had undergone a diagnostic laparoscopy and tubal patency test. Her ultrasound scan revealed low antral follicular count (AFC), and her Anti-Mullerian Hormone (AMH) was 0.2 ng/ml. She underwent transfer of two embryos using donor eggs and sperms of her partner after endometrial preparation. Her serum β hCG level on day 14 was 323 IU/L and was 711 IU/L after 48 hours suggestive of an intrauterine pregnancy. However, she presented with mild abdominal pain on day 26 of embryo transfer. Her ultrasound scan revealed no evidence of intrauterine pregnancy with a left adnexal mass measuring 2x2.5cm with minimal amount of free fluid in the POD. Since the initial assessment was highly suggestive of an ectopic pregnancy a diagnostic laparoscopy was performed and a ruptured left side ectopic with mild hemoperitoneum was found (Figure 1). Left side salpingectomy was performed since the right-side tube was healthy. Histology of the left side ruptured tube confirmed an ectopic pregnancy.



Figure 1. Ruptured left side tubal ectopic pregnancy.

Case 2

37 years old women with six years history of subfertility sought ART treatment after unsuccessful basic fertility treatment. She had severe endometriosis and underwent laparotomy for left ovarian endometrioma but otherwise without any medical comorbidities. The couple underwent ART with their gametes. Twelve eggs were retrieved, and ten embryos were developed by the ICSI method. She underwent frozen embryo transfer two months later due to the high risk of ovarian hyperstimulation syndrome after

ovum retrieval. Fourteen days after the transfer of the embryos, the β -hCG level was 223 IU/L and was 372IU/L after 48 hours. Serial beta HCG was planned due to the suboptimal rise of β -hCG. However, she presented with abdominal pain after two days, and ultrasound scan revealed no intrauterine pregnancy with a right sided unruptured ectopic pregnancy with minimal free fluid. Diagnostic laparoscopy revealed a leaking right side ectopic pregnancy with mild hemoperitoneum (Figure 2). Right side salpingectomy was performed, and the left side tube was disconnected as it was morphologically distorted with hydrosalpinx. Histology of the right-side tube confirmed the ectopic pregnancy.



Figure 2. Right side tubal ectopic pregnancy.

Discussion

The prevalence of EP following ART is varied, and individual risk factors could influence its occurrence. Several risk factors have been described for EP, especially following ART use of the large volume of culture medium during embryo transfer is one of them, which changes the hydrostatic pressure of moving the embryo through the tubal ostia and performing an embryo transfer close to the uterine fundus may increase the random fundal contraction when the catheter contact with the uterine fundus^{3,4}. In addition, Fresh embryo transfer, previous history of EP, previous pelvic or tubal surgery, endometriosis and pelvic inflammatory diseases have been shown to be associated with EP after ART⁵.

Apart from the theories explained about the possible mechanisms of EP after spontaneous conception, such as abnormal tubal function, tubal ciliary dysfunction, and altered tubal patency, several other pathomechanisms had been described for EP following ART. It includes overexpression of the adhesion molecule

E-cadherin in the tubal implantation sites due to overexpression of E-cadherin by embryos exposed to ART culture medium⁶. Due to control ovarian stimulation, hormonal changes affect the expression of signaling molecules such as cytokines, chemokines disrupting the interaction among embryo, fallopian tube and endometrium⁷. Moreover, immunologic changes and assisted hatching have also been associated with an increased risk of EP^{8,9}. All cases reported have assisted hatching before embryo transfer.

The management of EP involves conservative, medical and surgical depending on the clinical presentation and judgment. However, it is essential to consider the potential effects of different treatment options in terms of future fertility potential following the treatment, subsequent planning of ART treatment and its success. As a cytogenic drug, methotrexate could reduce ovarian reserve and affect ovarian response during future ovulation induction. However, studies have shown that it does not affect the ovarian reserve, with no difference in the mean number of oocytes collected after methotrexate treatment¹⁰. Adnexal blood supply may be affected following salpingectomy, and it could subsequently reduce the ovarian reserve¹¹. There are conflicting findings concerning surgical management of the ovarian reserve. However, studies have shown that there is no significant difference between patients who underwent ovarian induction pre- and post-salpingectomy¹².

In our cases, the first patient (Case 1) had no risk factors for EP, and her beta hCG also had doubled as for an intrauterine pregnancy. However, the case 2 had a history of endometriosis and distorted fallopian tube with a suboptimal rise of beta hCG. Salpingectomy was performed in both cases, and the contralateral tube was disconnected in the second case due to its appearance suggestive of hydrosalpinx. There is strong evidence to suggest that removal or disconnection of hydrosalpinx could improve the success rate of ART by preventing the direct toxic effect of the accumulated fluid on the transferred embryos through its leakage into the endometrial cavity¹³.

In conclusion, EP is a life-threatening emergency, and its incidence is increasing following ART. Serial serum beta hCG and pelvic sonographic screening facilitates early diagnosis and avoid the delay to initiate treatment irrespective of the risk factors for EP in ART patients. Though no one particular treatment modality is shown

to be superior, additional procedures namely contralateral salpingectomy may serve to reduce the recurrence of EP in future IVF cycles.

Disclosure

No conflict of interest in this case reports and informed written consent taken from both patients.

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