Case report-Olgu sunumu

# Tubal endometriosis as an insidious risk factor for tubal implantation in a procedure of assisted reproductive technique

Bir yardımcı üreme tekniği prosedüründe tubal implantasyon için sinsi bir risk faktörü olarak tubal endometriozis

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#### Abstract

Endometriosis is often associated with female infertility and exhibits a massive impairment in the physiology of uterine contractility that interferes with sperm and/or embryo movements. We present an unusual case of bilateral tubal pregnancy during an Invitro Fertilization-Embryo Transfer (IVF-ET) procedure in a tubal endometriosis patient. Bilateral tubal ampullary ectopic pregnancies, 20-30 milimeters in diameter were diagnosed during laparoscopic examination and bilateral salpingectomy was performed. Endometriotic implants were detected pathologically on mucosal surfaces of both tubes demonstrating the possible deleterious effect of endometriosis on embryo movement. Tubal mucosal environment containing endometriotic implants may behave like original uterine endometrium for ectopic tubal implantation of transferred embryos. However, we think that in order to decrease the probability for tubal implantation of transferred embryos; consideration of bilateral tubal closure or salpingectomy for patients with endometriosis before proceeding to an IVF-ET procedure may be useful.

Keywords: Pregnancy, ectopic, endometriosis, embryo transfer

#### Özet

Endometriozis çoğunlukla kadın infertilitesi ile ilişkilidir ve sperm ve/veya embriyo hareketlerini engelleyici, uterus kasılma fizyolojisinde belirgin bir bozulma ile kendini gösterir. Bir ender olgu olarak, İnvitro Fertilizasyon Embriyo Transferi (İVF-ET) prosedürü sırasında, bir tubal endometriozis hastasında bilateral tubal gebeliği sunduk. Laparoskopik değerlendirmede, 20-30 milimetre çapında bilateral tubal ampullada ektopik gebelik teşhis edildi ve bilateral salpenjektomi gerçekleştirildi. Endometriozisin, embriyo hareketini olası geciktirici etkisini gösteren, endometriyotik implantlar her iki tüpün mukozal yüzeylerinde patolojik olarak saptandı. Endometriyotik implantların oluşturduğu tubal mukozal ortam, transfer edilen embriyoların ektopik tubal implantasyonu için orijinal uterus endometriyumu gibi davranır. Bununla birlikte, biz, bir İVF-ET prosedürüne geçmeden önce, transfer edilen embriyoların tubal implantasyonu olasılığını azaltmak için, endometriozisli hastalara bilateral tubal kapama veya salpenjektomi uygulamasının göz önünde tutulmasının yararlı olabileceğini düşünmekteyiz.

Anahtar sözcükler: Gebelik, ektopik, endometriozis, embriyo transfer

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## Introduction

Ectopic pregnancy risk among Assisted Reproductive Techniques (ARTs) pregnancies varied according to ART procedure type, reproductive health characteristics of the woman carrying the pregnancy, and estimated embryo implantation potential [1]. In recent years, due to growing importance of ARTs, heterotopic implanted pregnancies like bilateral tubal pregnancy has been reported more frequently. Propulsion of gametes and embryos is achieved by complex interaction between muscle contractions, ciliary activity and the flow of tubal secretions. Evidence is accumulating about the important and possibly prominent role of ciliary motion in this process [2]. Endometriosis can probably be added to recently established risk factors for ectopic pregnancy. Endometriosis is often associated with female infertility and exhibits a massive impairment in the physiology of uterine contractility that interferes with sperm and/or embryo movements [3, 4]. The possible relationship between endometriosis and ectopic pregnancy during an invitro fertilization-embryo transfer (IVF-ET) procedure in a tubal endometriosis patient.

## **Case report**

A 33-year-old Turkish woman with 18 years of primary infertility was admitted to her first IVF-ET procedure for tubal factor infertility and mild endometriosis. She has previously been treated with clomiphene citrate for 6 cycles and 3 consecutive gonadotrophine plus intrauterine insemination procedures for unexplained infertility. Her second Hysterosalpingography (HSG) that was performed 6 months ago has revealed bilateral proximal tubal occlusion. Four endometriotic implants have been seen in the pelvic peritoneum during diagnostic laparoscopy that was performed 3 months ago for infertility work-up based on her abnormal HSG result. Chromopertubation of uterine tubes with methylene dye during laparoscopy confirmed bilateral proximal tubal occlusion and her endometriotic implants have also been coagulated with bipolar cautery. Past history of the patient was uneventful, having no sexual transmitted diseases or pelvic inflammatory disease except a previously performed appendectomy. Recombinant follicle stimulating hormone (150 IU/Day) and human menopausal gonadotrophin (225 IU/Day) were started on the first cycle day and administered for 10 and 8 days, respectively. Four embryos, consisting 2 in grade I and 2 in grade II, were transferred to uterine cavity without any difficulty with soft transfer catheter by intracytoplasmic sperm injection, 3 days after fertilization.

Twenty days after embryo transfer she was admitted to the emergency department complaining of pelvic pain and vaginal bleeding. Transvaginal ultrasonography established a right tubal ectopic ring, 28 milimeter in diameter without intrauterine gestational sac. One day after admission to the clinic,  $\beta$ -hCG level increased from 530 to 590 mIU/ml and the patient developed intraabdominal bleeding signs and hypovolemic shock symptoms.

During laparoscopic examination, bilateral tubal ampullary ectopic pregnancies, 20-30 milimeters in diameter were diagnosed. Bilateral salpingectomy was performed and pathological examination confirmed bilateral tubal ectopic pregnancy containing endometriotic implants (Figures 1-3). The glands of endometriosis lined by flattened epithelial cells and stroma exhibiting marked decidual transformation, nests of endometriotic glands and stroma, chorionic villi within dilated tube lumen were prominent pathological findings demonstrating tubal endometriosis.

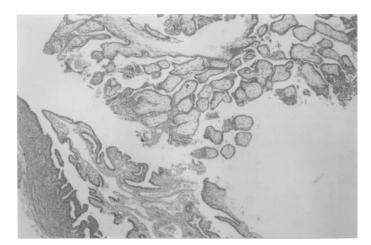


Figure 1: Chorionic villi within dilated tube lumen (Haematoxylin and Eosin, Original magnification, 50x).

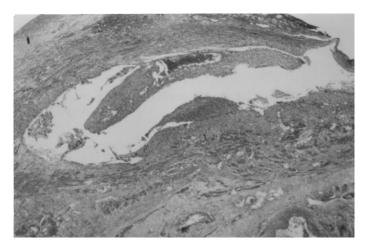


Figure 2: Endometriosis gland lined by flattened epithelial cells and stroma exhibiting marked decidual transformation (Haematoxylin and Eosin, Original magnification, 100x).

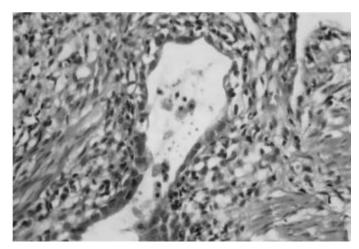


Figure 3: A nest of endometriotic gland and stroma (Haematoxylin and Eosin, Original magnification, 200x).

### Discussion

Bilateral ectopic pregnancy is a very rare condition occuring mostly with ART. 1/725-1/1580 of all ectopic pregnancies are reported as bilateral [5, 6]. There are possible mechanisms responsible for ectopic pregnancy pathogenesis following IVF-ET. Transfer of embryos directly to the tube is one of them [7]. The volume of the transfer medium has been considered to be of great importance. The "spray effect" theory has been proposed, inherent qualities of transfer medium may lead to dispersion of the embryos to seperate directions even with right placement of the catheter tip. Spontaneous migration of embryos to the tubes with the carrier effect of uterine fluid in a retrograde way due to junctional zone contractions is also a possible mechanism. When tubal pathology is diagnosed as the exact cause of infertility, bilateral salpingectomy or bilateral tubal closure before IVF-ET is advised [8]. Tubal pregnancy associated with tubal endometriosis can also be treated successfully with laparoscopical administration of methotrexate and temporarily used gonadotropin releasing hormone analogues postoperatively [9]. One explanation for tubal implantation is the tubal mucosal environment resembling the native endometrium of endometriotic patient [10]. Increased progesterone in the luteal phase of menstrual cycle favors prostaglandin-E that relaxes isthmic portion of the fallopian tube allowing the fertilized ovum into the uterine cavity. Tubal prostaglandin production is also altered in endometriosis [11, 12]. Ovulation induction with clomiphene citrate or injectable gonadotropin therapy has been linked with a 4-fold increase in the risk of ectopic pregnancy in a case-control study. This finding suggests that multiple eggs and high hormone levels may be significant factors. The risk of ectopic pregnancy and heterotopic pregnancy (pregnancies occurring simultaneously in different body sites) dramatically increases when a patient has used assisted reproductive techniques to conceive. Approximately 1% of pregnancies achieved through IVF or Gamete Intrafallopian Transfer (GIFT) can result in a heterotopic gestation, compared to an incidence of 1 in 30.000 pregnancies for spontaneous conceptions. In a study of 3000 clinical pregnancies achieved through in vitro fertilization, the ectopic pregnancy rate was 4.5%, which is more than double the background incidence [13]. This case demonstrates endometriotic implants pathologically and increases the evidence of the overlap between endometriosis and ectopic pregnancy. Retrospective pathological studies are also needed for the determination of this possible relationship.

Consequently, tubal mucosal environment with endometriotic implants resembling original uterine endometrium can be a risk factor for ectopic implantation of transferred embryos during an IVF-ET procedure. Although diagnosis of tubal endometriosis is not always easily established; before proceeding to an IVF-ET procedure for infertility management of the patients with endometriosis, bilateral tubal closure or salpingectomy can be considered to decrease the chance for unwanted tubal implantations of transferred embryos.

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## References

- 1. Clayton HB, Schieve LA, Peterson HB, Jamieson DJ, Reynolds MA, Wright VC. Ectopic pregnancy risk with assisted reproductive technology procedures. Obstet Gynecol 2006; 107: 595-604.
- 2. Lyons RA, Saridogan E, Djahanbakhch O. The reproductive significance of human Fallopian tube cilia. Hum Reprod Update 2006; 12: 363-72.
- 3. Kissler S, Zangos S, Wiegratz I, Kohl J, Rody A, Gaetje R, Doebert N, Wildt L, Kunz G, Leyendecker G, Kaufmann M. Utero-tubal sperm transport and its impairment in endometriosis and adenomyosis. Ann N Y Acad Sci 2007; 1101:

38-48.

- 4. Vegheş S, Lupaşcu I, David C, Vişan V, Vasiliu V. Specifics of therapy of tubal infertility in patients with endometriosis. Rev Med Chir Soc Med Nat Iasi 2005; 109: 542-7.
- 5. Yoo JK, Lee JJ, Song JH, Jeon SC, Kang JH, Kim S, Park CH, Cho DH. A case of simultaneous bilateral tubal pregnancies following the ovulation induction and intrauterine insemination. Korean J Obstet Gynecol 2001; 44: 2372-5.
- 6. Kauppi-Sahla M, Rintala H, Mäkinen J. Bilateral tubal pregnancy: a case report and review of the literature. Eur J Obstet Gynecol Reprod Biol 1991; 40: 145-7.
- 7. Aanesen A, Flam F. Bilateral tubal pregnancy following in vitro fertilization and transfer of two embryos. Eur J Obstet Gynecol Reprod Biol 1996; 64: 235-6.
- 8. Klipstein S, Oskowitz SP. Bilateral ectopic pregnancy after transfer of two embryos. Fertil Steril 2000; 74: 887-8.
- Sánchez Contreras J, Hernández Vivar LE, Villalobos Cid MA, Risco Cortés RJ. Conservative treatment of interstitial ectopic pregnancy and endometriosis with laparoscopic methotrexate and potassium chloride and complementary management with nasal nafarelin. Report of a case and review of the literature. Ginecol Obstet Mex 2000; 68: 35-8.
- 10. Hunter RH. Tubal ectopic pregnancy: A patho-physiological explanation involving endometriosis. Hum Reprod 2002; 17: 1688-91.
- 11. Nabekura H, Koike H, Ohtsuka T, Yamaguchi M, Miyakawa I, Mori N. Fallopian tube prostaglandin production with and without endometriosis. Int J Fertil Menopausal Stud 1994; 39: 57-63.
- 12. Bogdanskiene G, Berlingieri P, Grudzinskas JG. Association between ectopic pregnancy and pelvic endometriosis. Int J Gynaecol Obstet 2006; 92: 157-8.
- 13. Marcus SF, Brinsden PR. Analysis of the incidence and risk factors associated with ectopic pregnancy following in-vitro fertilization and embryo transfer. Hum Reprod 1995; 10: 199-203.