

배란 유도 후 발생한 난관상태 임신

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Live twin tubal ectopic pregnancy after ovulation induction

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Twin tubal ectopic pregnancy is rare. Especially the live twin tubal ectopic pregnancy is extremely rare, just 10 cases have been reported until now.

There were 9 cases of live twin tubal pregnancy after spontaneous conception and one case after IVF cycle. This is the first report of live twin tubal ectopic pregnancy after ovulation induction with clomiphene citrate. A 31-year-old woman, nulligravida complained of primary infertility and irregular menstruation. After ovulation induction with clomiphene citrate, β -hCG was 1566 mIU/mL on missed period of 5 weeks 4 days. On 6⁺ weeks, β -hCG was elevated to 3446 mIU/mL and transvaginal ultrasound revealed two separated gestational sacs, each containing yolk sac in the left tube. The variable dose of methotrexate therapy was tried using 1 mg/kg of methotrexate and 0.1 mg/kg of leukovorin. These were injected alternatively for 8 days. On 7⁺ weeks, β -hCG was elevated to 8,029 mIU/mL and transvaginal ultrasound revealed two fetal poles with heart beat in each gestational sacs. Laparoscopic salpingectomy was performed. The diagnosis was confirmed by the operative finding and also in the pathologic report. It is needed that careful ultrasonographic examination especially in the case of ovulation induction or IVF-ET. Methotrexate treatment in twin tubal pregnancy was usually failed. There was only one successful report by the direct injection of methotrexate to the fallopian tube combined with single intramuscular injection. Further research for dosage or route of administration will be needed.

Key Words: Live twin tubal ectopic pregnancy, Ovulation induction

Twin tubal ectopic pregnancy is a rare diagnosis with an incidence of 1: 200 ectopic pregnancies. The incidence of live tubal twin ectopic pregnancy is even rarer, has been calculated to be 1: 125,000 pregnancies.^{1,2} The first published case of unilateral twin ectopic pregnancy was reported by De Ott³ in 1891. Since

then, more than 100 cases of twin ectopic pregnancy have been reported. However, live twin tubal pregnancy that is fetal cardiac motion in both embryos visualized with transvaginal sonography have been reported only 10 cases.^{2,4,5} The first of these was reported by Gualandi et al.⁶ in 1994. As the incidence of ectopic pregnancy and heterotypic pregnancy has increased since the advent of ovulation induction, in vitro fertilization-embryo transfer, and prevalent sexual transmitted disease and pelvic inflammatory disease, the incidence of twin tubal ectopic pregnancy might be in-

접 수 일 : 2009. 3. 20.
채 택 일 : 2009. 9. 8.
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* The abstract was presented in 11th world congress on Controversies in Obstetrics and Gynecology and Infertility (Paris, France, 2008).

creased also.⁷ There were 9 cases of live twin tubal pregnancy after spontaneous conception and one case after IVF cycle.⁸ This is the first report of live twin tubal ectopic pregnancy after ovulation induction with clomiphene citrate. We describe a case of unilateral dichorionic twin ectopic pregnancy, which was failed to treat with methotrexate.

Case Report

A 31-year-old woman, nulligravida complained of primary infertility and irregular menstruation. Through the infertility work up, the final diagnosis was chronic anovulation, endometrial complex hyperplasia without cytologic atypia, and polycystic ovarian syndrome. The patient had no history of any major illnesses or surgeries. She was not using any contraceptive devices and she didn't have any history of abortion. After cyclic progestin treatment for 6 months, ovulation induction could be scheduled.

The ovulation induction was performed with clomiphene citrate 50 mg for 5 days. Two growing follicles in the left ovary were observed during the ultrasonography monitoring. After confirming the ovulation by urinary luteinizing hormone kit, timed sex-

ual contact was recommended. On missed period of 5weeks 4days, the β -hCG was 1566 mIU/mL. The β -hCG was elevated to 3,446 mIU/mL on 6⁺¹ weeks, however, transvaginal ultrasound revealed a bulky empty uterus. There was two separated gestational sacs, each containing yolk sac in the left tube. She had vaginal spotting but did not have the abdominal pain or tenderness. So the variable dose of methotrexate therapy was tried using 1 mg/kg of methotrexate and 0.1 mg/kg of leukovorin. There were injected alternatively for 8 days. But the β -hCG was elevated to 6,790 mIU/mL on 6⁺⁵ weeks. On 7⁺³ weeks, the β -hCG was elevated to 8,029 mIU/mL and transvaginal ultrasound revealed two fetal poles with heart beat in each gestational sacs (Fig. 1). Unfortunately methotrexate treatment was not effective, laparoscopic left salpingectomy was performed. At the time of laparoscopy, two sacculated mass on left tube was found (Fig. 2). The left tube was not ruptured and there was no active bleeding from the tube. The other tube was apparently normal. The woman was discharge home the following morning. The histological examination of the specimen confirmed unilateral tubal twin pregnancy (Fig. 3).



Fig. 1. Transvaginal ultrasound revealed two fetal poles with heart beat in each gestational sacs.

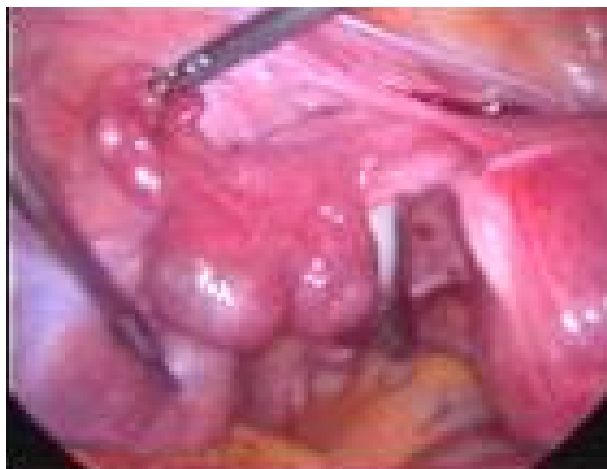


Fig. 2. At the time of laparoscopy, two sacculated mass on left tube was found. The left tube was not ruptured or there was no active bleeding from the tube. The other tube was apparently normal.

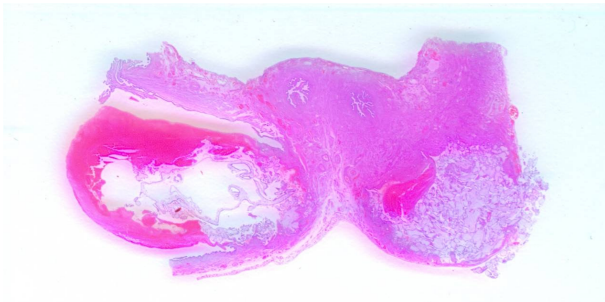


Fig. 3. The histological examination of the specimen confirmed unilateral tubal twin pregnancy. The gestational tissues were apparently apart from each other (H&E, $\times 10$).

Discussion

The incidence of ectopic pregnancy is progressively increasing and is estimated as 1~2%.⁹ Live twin tubal pregnancy are extremely rare. However, as the incidence of ectopic pregnancy and heterotypic pregnancy has increased since the advent of ovulation induction, in vitro fertilization-embryo transfer, and prevalent sexual transmitted disease and pelvic inflammatory disease, the incidence of twin tubal ectopic pregnancy might be increased also.⁷ The concern is come true and this is the first report of live twin tubal pregnancy after ovulation induction with clomiphene citrate. In the absence of an intrauterine gestational sac in the presence of a normally rising β -hCG titer, a diagnosis of multiple ectopic gestation should be considered.^{2,10} This case concurred with those reports. In recent years, transvaginal sonography has dramatically improved the accuracy of the diagnosis of ectopic pregnancy.⁴ Although the incidence of ectopic pregnancy has increased dramatically in the past 30 years, the maternal fatality has dropped by nearly 90% with the advent of early sonographic detection and highly sensitive serum β -hCG tests.¹

Most of twin tubal pregnancies were thought to be monozygotic monochorionic, with a single decidual sac containing two embryos, even though majority of them

was determined subjectively by using ultrasonographic criteria. Neuman et al.¹¹ reported results indicative of a dizygotic twin with the use of DNA probes for restriction fragment length polymorphisms which was the only objective way to assess it. In this case, the pregnancy was dichorionic twin with two separated sacs, each containing a fetal pole with cardiac activity by ultrasonography. And two separated placentas were confirmed also by the histologic examination. Considering the condition of ovulation induction, it could be dizygotic twin but was not confirmed by karyotypic study.

The medical treatment with methotrexate for ectopic pregnancy became comparable with salpingostomy if the early diagnosis was made.¹² But in the twin tubal pregnancy, a single dose of methotrexate therapy may be insufficient for conservative therapy.¹³ In our case, we started the injection of methotrexate in the good condition that was relatively low β -hCG level (3,446 mIU/mL), on 6⁺¹ gestational weeks, without fetal heart beat. And the variable multiple dose of methotrexate therapy was tried. However it was failed. There was only one report of unilateral twin tubal pregnancy without heart beat treated by a combination of local and systemic administration of methotrexate.¹⁴ Fernandez et al.¹⁴ explained local methotrexate treatment with ultrasound guidance allowed a relatively high tissue concentration when methotrexate was administered directly into the sac. Further research for dosage or route of administration will be needed. In the live twin tubal pregnancy, all reported cases have been managed via laparotomy or laparoscopy.

The live twin tubal pregnancy is extremely rare. We report a case of unilateral dichorionic twin ectopic pregnancy after ovulation induction, which was failed to treat with methotrexate, and treated finally by laparoscopic salpingectomy.

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= 국문초록 =

난관 쌍태임신은 드문 질환으로서, 특히 심박동이 있는 경우는 더욱 드물어서 단지 10예만이 보고된 바 있으며 현재까지 국내 보고는 없다. 지금까지의 9예는 자연임신에 의한 것이고, 한 예는 체외수정술 후 발생한 것으로서, 배란유도 후 발생한 난관 쌍태임신은 보고된 바 없다. 저자 등은 일차성 불임과 월경불순으로 내원한 31세 미임신부에서 클로미펜으로 배란유도를 시행한 후 무월경 5주 3일에 β -hCG 1,566 mIU/mL로 임신이 확인되었다. 임신 6주 1일에 β -hCG는 3,466 mIU/mL로 상승하였으나, 경질초음파에서 자궁강내 임신낭을 발견할 수 없었고, 좌측 난관에 각각의 난황낭을 포함한 두개의 임신낭이 관찰되었다. methotrexate 다회요법이 시도되었으나, 임신 7주 3일에 β -hCG는 8,028 mIU/mL로 상승되었고 초음파검사에서도 태아심박동이 관찰되었다. 복강경하 좌측난관절제술이 시행되었으며, 술후 조직검사상 일측 난관 쌍태임신이 확인되었다. 난관 쌍태임신에서 methotrexate치료는 대개 실패하였으며, 단지 난관내 직접 주입과 근육주사를 병행한 한 예에서만 성공하였다. 따라서 난관 쌍태임신 시 약물치료는 향후 약제 용량이나 투여경로에 관한 연구가 필요할 것으로 사료된다. 저자 등은 배란유도 후 발생한 심박동이 있는 난관 쌍태임신을 간단한 문헌고찰과 함께 보고하는 바이다.

중심단어: 난관 쌍태임신, 배란유도