

CONSERVATIVE LAPAROSCOPY FOLLOWING PROPHYLACTIC METHOTREXATE FOR AN UNRUPTURED BILATERAL TUBAL PREGNANCY

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Bilateral simultaneous tubal pregnancy is a rare event. Conservative treatment is the standard method to preserve fertility. This report describes the use of a combination of laparoscopic salpingostomy and postoperative prophylactic methotrexate (MTX) in a woman with bilateral tubal pregnancy in order to preserve fertility successfully.

A 25-year-old woman, gravida 1, para 0, abortus 1, suffered from secondary amenorrhea combined with intermittent vaginal bleeding and dull lower abdominal pain 1 week before she was referred to our medical center. Her gynecologic history showed secondary infertility of more than 1 year. There was no history of pelvic inflammatory disease, intrauterine contraceptive device use, or major pelvic surgery. Urinary pregnancy test was positive after the second course of clomiphene citrate (Clomid; YunHsin, Taichung, Taiwan), with 100 mg administered orally, from days 5–9 of the menstrual cycle at a private clinic. However, no intrauterine pregnancy was revealed on serial ultrasonography. Serum human chorionic gonadotropin (hCG) level showed an abnormal rise (11,000 IU/L initially vs. 17,000 IU/L 4 days after initial measurement). She was then transferred to our tertiary center. Vaginal ultrasound scan was performed, confirming the absence of a gestational sac in the uterus and showing the presence of abdominal fluid and a right adnexal mass measuring 3.2×2.8 cm.

Laparoscopic surgery was arranged under the impression of extrauterine pregnancy. In the operating room, about 200 mL of blood was found in the cul-de-sac. Both tubes had an ampullary pregnancy (Figure).

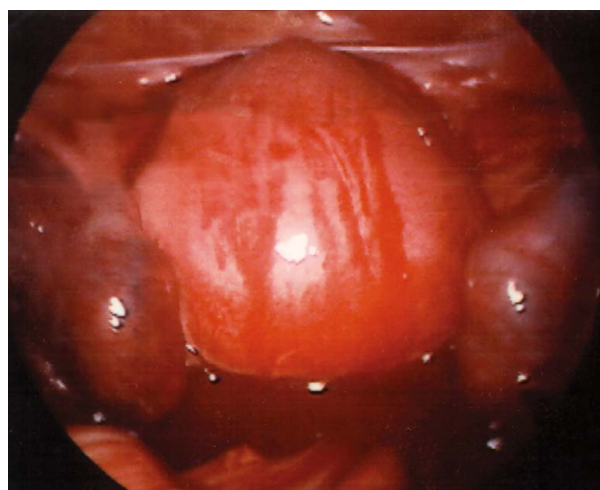


Figure. Unruptured bilateral tubal pregnancy, both in the ampullary portion.

A clinical diagnosis of bilateral ectopic pregnancy was made. Laparoscopic bilateral salpingostomy with removal of the products of conception was carried out to preserve tubal fertility.

Prophylactic MTX (AHP Pharma, Hoofddorp, The Netherlands) treatment is indicated, because the pre-operative serum hCG level was more than 10,000 IU/L. Since there was no contraindication for the use of MTX after serial laboratory workup, prophylactic MTX was administered as a single dose of 1 mg/kg intramuscularly (total dose 50 mg), within 24 hours postoperatively. No side effects related to MTX were noted. The postoperative condition was uneventful. The patient was discharged as scheduled.

Serum hCG level declined to 1,105 IU/L 3 days after the administration of MTX. Urinary pregnancy test result was negative 3 weeks after surgery. Histologic examination of the specimens from the bilateral tubes confirmed the diagnosis. Spontaneous conception was diagnosed 11 months after surgery. A normal healthy



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girl weighing 3,210 g was born at 39 weeks' gestation via normal spontaneous vaginal delivery.

Bilateral simultaneous tubal pregnancy is a rare event. The estimated incidence of bilateral simultaneous tubal pregnancy is 1/200,000 of live births following natural conception [1] and 1/725 to 1/1,580 of all extrauterine pregnancies [2]. Kauppi-Sahla et al [3] demonstrated the association between bilateral tubal pregnancies and clomiphene use. Our patient had received clomiphene citrate for ovulation induction, and this may have resulted in multiple ovulation. Therefore, clinicians must be alert to the possibility of bilateral tubal pregnancy in patients who receive clomiphene citrate. Additionally, bilateral tubal pregnancies have been reported in natural cycles [4], after *in vitro* fertilization [5,6], and use of an intrauterine contraceptive device following tubal surgeries (both sterilization and reversal of sterilization operations) [7]. Recently, the incidence has increased, because both pelvic inflammatory disease and the use of assisted fertility have become more common [8,9].

The clinical diagnosis of bilateral tubal pregnancy is similar to unilateral ectopic pregnancy, including the symptoms and/or signs, and the abnormal serum hCG levels in comparison with a normal pregnancy. Like most reported cases, our preoperative survey failed to reveal bilateral ectopic pregnancy. The typical sonographic findings indicative of right ectopic pregnancy failed to alert us to the possibility of a left ectopic pregnancy, and we did not detect the concomitant left ectopic pregnancy, in the presence of the abnormally high serum hCG levels. Thus, clinicians must keep in mind the importance of inspecting the contralateral tube at the time of preoperative sonographic examination and surgery in patients after the use of ovarian stimulants.

The standard treatment for unruptured unilateral ectopic pregnancy in women who wish to preserve their fertility includes salpingostomy and medical MTX treatment. The literature revealed that there were no differences between laparoscopy and medical treatment in terms of the primary success rate, the homolateral tubal patency rate [10], and subsequent fertility outcomes [11]. However, laparoscopy has more advantages over medical treatment. Failed primary MTX treatment at the dose of 50 mg/m² for unrecognized bilateral tubal pregnancy was reported [12], and it is proposed that the effective dosage of systemic MTX for bilateral tubal pregnancy should be adjusted. In addition, a definite diagnosis of bilateral tubal pregnancy was not made until surgery was performed. Laparoscopy is the most common minimally invasive surgery. Since subsequent spontaneous conception in women after unruptured bilateral tubal pregnancy

treated with laparoscopic salpingostomy was published, laparoscopic conservative surgery has remained the cornerstone of treatment [13].

Stovall et al [14] first addressed the single-dose MTX for treatment of ectopic pregnancies in 1991. Later, this group reported that high preoperative serum hCG levels was significantly linked to the failure of medical treatment [15]. They found that among the women with initial serum hCG of more than 10,000 IU/L, the failure rate was nearly 25%. They concluded that among women with tubal ectopic pregnancies, high serum hCG was the most important factor associated with failure of treatment with a single-dose MTX protocol.

In addition, risk factors associated with persistent ectopic pregnancies after conservative surgery includes high preoperative hCG levels (>3,000 IU/L), daily changes of preoperative increasing hCG levels >100 IU/L, and postoperative day 7 hCG levels >1,000 IU/L [16,17]. Graczykowski and Mishell [18] demonstrated that the prophylactic postoperative MTX regimen (a single dose of 1 mg/kg intramuscularly, within 24 hours postoperative) can be used to significantly reduce the incidence of persistent ectopic pregnancy after linear salpingostomy from 14.5% to 1.9%. Furthermore, it shortened the postoperative follow-up period. Postoperative prophylactic MTX may be recommended in high-risk cases.

A review of the literature showed that all preoperative serum hCG levels in cases of bilateral tubal pregnancy successfully treated with laparoscopic salpingostomy were either less than 3,000 IU/L or not revealed. In our case, the preoperative hCG level was more than 10,000 IU/L, and daily increases of preoperative hCG level were more than 100 IU/L. The incidence of persistent ectopic pregnancy after laparoscopic surgery was estimated to be more than 14.5% in our case. Thus, a single dose of prophylactic MTX (1 mg/kg) was administered intramuscularly in our case to preserve fertility. It resulted in sequent patent unilateral tube and spontaneous conception later.

In conclusion, laparoscopic conservative surgery is the cornerstone of treatment in women with unruptured bilateral ectopic pregnancies. In addition, a single dose of prophylactic MTX (1 mg/kg) within 24 hours given postoperatively is recommended to preserve fertility in women at high risk of developing persistent ectopic pregnancies.

References

1. Edelstein MC, Morgan MA. Bilateral simultaneous tubal pregnancy: case report and review of the literature. *Obstet Gynecol Surv* 1989;44:250-2.

2. Abrams RA, Kanter AE. Bilateral simultaneous extrauterine pregnancy. *Am J Obstet Gynecol* 1948;56:1198-200.
3. 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.
4. De Graaf FL, Demetroulis C. Bilateral tubal ectopic pregnancy: diagnostic pitfalls. *Br J Clin Pract* 1997;51:56-8.
5. Campo S, Campo V, Gambadauro P. Bilateral tubal pregnancy following in vitro fertilization and embryo transfer. *Eur J Obstet Gynecol Reprod Biol* 2003;110:237-9.
6. Wang YL, Yang TS, Chang SP, Ng HT. Heterotopic pregnancy after GIFT managed with expectancy: a case report. *Chin Med J* 1996;58:218-22.
7. Klipstein S, Oskowitz SP. Bilateral ectopic pregnancy after transfer of two embryos. *Fertil Steril* 2000;74:887-8.
8. Serour GI, Aboulghar M, Mansour R, Sattar MA, Amin Y, Aboulghar H. Complications of medically assisted conception in 3,500 cycles. *Fertil Steril* 1998;4:638-42.
9. Strandell A, Thorburn J, Hamberger L. Risk factors for ectopic pregnancy in assisted reproduction. *Fertil Steril* 1999;71:282-6.
10. Hajenius PJ, Engelsbel S, Mol BW, et al. Randomised trial of systemic methotrexate versus laparoscopic salpingostomy in tubal pregnancy. *Lancet* 1997;350:774-9.
11. Dias Pereira G, Hajenius PJ, Mol BW, Ankum WM, Hemrika DJ, Bossuyt PM, van der Veen F. Fertility outcome after systemic methotrexate and laparoscopic salpingostomy for tubal pregnancy. *Lancet* 1999;353:724-5.
12. Marcovici I, Scoccia B. Spontaneous bilateral tubal ectopic pregnancy and failed methotrexate therapy: a case report. *Am J Obstet Gynecol* 1997;177:1545-6.
13. Sommer EM, Reisenberger K, Bogner G, Nagele F. Laparoscopic management of an unrecognized spontaneous bilateral tubal pregnancy. *Acta Obstet Gynecol Scand* 2002;81:366-8.
14. Stovall TG, Ling FW, Gray LA. Single-dose methotrexate for treatment of ectopic pregnancy. *Obstet Gynecol* 1991;77:754-7.
15. Lipscomb GH, McCord ML, Stovall TG, Huff G, Portera SG, Ling FW. Predictors of success of methotrexate treatment in women with tubal ectopic pregnancies. *N Engl J Med* 1999;341:1974-8.
16. Lunderoff P, Hahlin M, Sjoblom P, Lindblom B. Persistent trophoblast after conservative treatment of tubal pregnancy: prediction and detection. *Obstet Gynecol* 1991;77:129-33.
17. Hagstrom HG, Hahlin M, Bennegard-Eden B, Sjoblom P, Thorburn J, Lindblom B. Prediction of persistent ectopic pregnancy after laparoscopic salpingostomy. *Obstet Gynecol* 1994;84:798-802.
18. Graczykowski JW, Mishell DR Jr. Methotrexate prophylaxis for persistent ectopic pregnancy after conservative treatment by salpingostomy. *Obstet Gynecol* 1997;89:118-22.