Nonsurgical Management with Methotrexate Treatment of Recurrent Ectopic Pregnancy in a Primary Infertile Patient (A Case Report)

REKÜRREN EKTOPİK GEBELİĞİN METOTREKSAT İLE TEDAVİSİ

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Summary

We report a case on a 38 year old primary infertil woman gravida 5, para 0 who complained, after seven weeks of amenorrhea of vaginal bleeding and subacute pain in the lower abdomen. She had undergone left linear salpingotomy because of left unruptured pregnancy in June 1994 and single-dose per oral methotrexate therapy because of right unruptured tubal pregnancy in September 1999 consequtively. As a third time a non ruptured left tubal pregnancy was recognised at transvaginal ultrasonography single dose methotrexate was administered intramuscular and subsequently, serum human chorionic gonadotropin (hCG) was quantified every two days. After a brief rise, hCG concentration dropped continuously down and was no longer detectable after two months. Tubal patency on both sides was demonstrated by hysterosalpingogram done three months after the therapy. We conclude that the methotrexate use is safe and effective in treatment of recurrent tubal ectopic pregnancy.

Key Words: Tubal pregnancy, Methotrexate

T Klin J Gynecol Obst 2000, 10:208-210

Özet

Ocak 1999'da 38 yaşındaki primer infertil hasta yedi hafta süren amenore ve alt karında subakut ağrı yakınması ile başvurdu. Anamnezinde Haziran 1994'de sol rüptüre olmamış gebelik nedeniyle sol lineer salpingotomi ve Eylül 1994'de sağ rüptüre olmamış gebelik nedeniyle peroral metotreksat tedavisi vardı. Transvaginal ultrasonografide bozulmamış sol tubal ektopik gebelik tanısı konan hastaya tek doz intramüsküler metotreksat tedavisi verilerek serum human koryonik gonadotropin (hCG) düzeyi iki günde bir ölçüldü. Kısa süreli bir artış sonrası serum hCG düzeyi sürekli olarak azaldı ve iki ay sonra ölçülemez düzeylere indi. Üç ay sonra yapılan histerosalpingografide her iki tuba açık olarak izlendi. Tekrar eden tubal ektopik gebeliklerde metotreksat kullanımı güvenli ve etkili bir yöntemdir.

Anahtar Kelimeler: Tubal gebelik, Metotreksat

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After an ectopic pregnancy, there is a 7 to 13 fold of increase in the risk of a subsequent ectopic pregnancy. The chance that a subsequent pregnancy will be intrauterine is 50-80%; and the chance that the pregnancy will be tubal is 10-25%; the remaining patients will be infertile. Many variables make accurate assessment of risk very difficult. (eg, size and location of the ectopic pregnancy, status of the contralateral adnexa, treatment method, and history of infertility) (1-3). Tubal damage results from inflammation, infection and surgery. Inflammation and infection may cause damage without complete tubal obstruction. Complete blockage may result from salpingitis, incomplete tubal ligation, tubal fertility surgery, partial salp-

Geliş Tarihi: 15.09.1999

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Bu vaka takdimi, 19-22 Mayıs tarihleri arasında Antalya'da yapılan 3. Türk-Alman Jinekoloji-Obstetri Kongresinde poster olarak sunulmuştur.

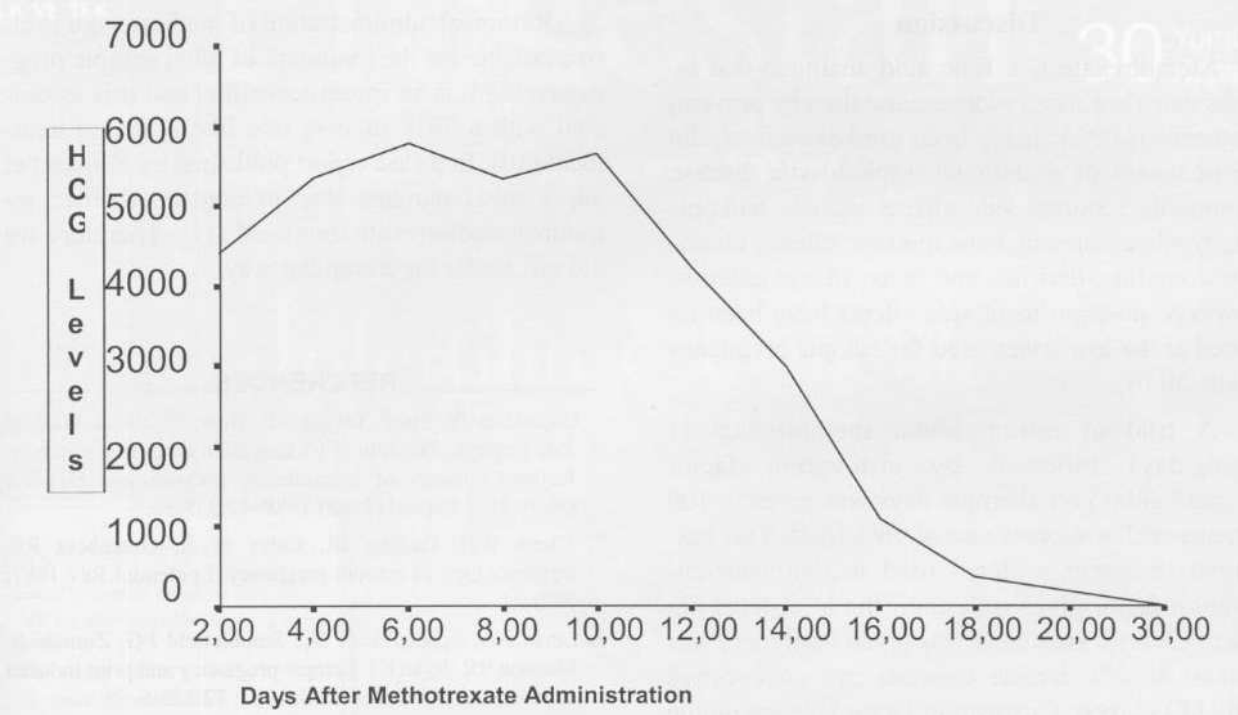

Figure 1. HCG levels of the patient after methotrexate administration.

ingectomy, or congenital midsegment tubal atresia. Damage to mucosal portion of the tube or fimbria accounts for about one-half of all tubal pregnancies (4).

Although the incidence of ectopic pregnancy increases with increasing age and parity, there is also a significant increase in nulliparous women undergoing infertility treatment. For nulliparous women, conceptions after at least one year of unprotected intercourse are 2-6 times more likely to be tubal. Additional risk for infertile women are associated with specific treatments, including reversal sterilisation, tuboplasty, ovulation induction and in vitro fertilization. Hormonal alterations characteristic of clomiphen citrate and gonadotropin ovulation induction cycles may predispose tubal implantation. About 1,1-4,6% conceptions associated with ovulation induction are ectopic pregnancies (2-5). In many of these patients, the results of hysterosalpingography are normal and there is no evidence of intraoperative tubal pathology.

Case Report

A 38 year-old primary infertile woman gravida 5 para 0, who complained, after seven weeks of amenorhea, of vaginal bleeding and subacute pain in the lower abdomen was admitted to Ege University Gynecology Department in January 1999. She had undergone left linear salpingotomy because of left unruptured pregnancy in June 1994 and single dose per oral methotrexate therapy because of right unruptured tubal pregnancy in September 1994. Physical examination was unremarkable. As a third time a non-ruptured left tubal pregnancy was recognised at transvaginal ultrasonography again. On the ultrasonographic examination, the endometrial thickness was 11 mm. and fetus was not observed in the uterine cavity but a non-ruptured left tubal pregnancy was recognised adjacent to the nongravid uterus. The hCG level was 4300 mIU/ml. Single dose methotrexate (1mg/kg) was administered intramuscular and subsequently, hCG was quantified every two days. After a brief rise, the hCG concentration dropped continuously down and was no longer detectable after two months (Figure 1). No side effects was observed. Tubal patency on both sides was demonstrated by hysterosalpingogram done three months after the therapy.

Discussion

Methotrexate is a folic acid analogue that inhibits dehydrofolate reductase and thereby prevents synthesis of DNA. It has been used extensively for the treatment of gestational trophoblastic disease. Commonly reported side effects include leukopenia, trombocytopenia, bone marrow aplasia, ulcerative stomatitis, diarrhea and hemorrhagic enteritis. However, no significant side effects have been reported at the low doses used for ectopic pregnancy treatment (6).

A trial of intramuscular methotrexate (1 mg/kg/day) followed by citrovarum factor (0,1mg/kg/day) on alternate days was given to 100 patients with a success rate of 96% (6,7). This outpatient treatment protocol used methotrexate/citrovarum factor given only until the hCG level began to decline. Treatment was given until there was at least a 15% decline between two concecutive daily hCG levels. Citrovarum factor is given on the day after the methotrexate administrated, even if no further methotrexate is indicated. Once methotrexate is discontinued, hCG levels are measured weekly until the results are negative. A second course of methotrexate/citrovarum factor is given only if there is a plateau or rise in the hCG level. On the 96 patients successfully treated, 17 required only one methotrexate/citrovarum factor dose and, 19 required four doses. Four patients treated with methotrexate failed therapy and required surgical treatment for tubal rupture, and each of these cases was different with respect to ectopic pregnancy size, hCG level, and time of rupture.

Reproductive function after methotrexate treatment can be assessed on the basis of tubal pregnancy. Tubal patency is reported to be 50-100%, with a mean of 71%, after systemic methotrexate treatment. In two separate reports of 23 and 62 patients, the tubal patency rate on the ipsilateral side was 81,4% and 82,3% respectively (8,9).

Intratubal administration of methotrexate is also available for the treatment of tubal ectopic pregnancy, but it is an invasive method and it is associated with a 70% success rate like systemic treatment (10). In a case report published by Klinkert et all, a tubal damage was demonstrated after intratubal methotrexate treatment (11). Therefore we did not prefer the intratubal way.

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