

# Successful Treatment of Cervical Pregnancy with Methotrexate Administration: A Case Report

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A case of cervical pregnancy which was successfully treated by intramuscular methotrexate therapy is presented. It is suggested that, in cervical pregnancies in which fertility preservation is desired, medical treatment would be applied if the patient condition is proper.

**Key Words:** Cervical pregnancy, Methotrexate, Fertility preservation

*Gynecol Obstet Reprod Med;14:2 (113 - 115)*

## Introduction

Cervical pregnancy is a rare form of ectopic pregnancy which is often associated with significant morbidity and devastating effects on future fertility. It accounts for, 1 % of all ectopic gestations. Its incidence varies between 1 in 1000 to 16 000 pregnancies, with the highest figures reported from Japan, which also has a high incidence of antecedent curettage.<sup>1</sup> The diagnosis of cervical pregnancy is commonly delayed and is often made intraoperatively in the presence of massive blood loss, necessitating an emergency hysterectomy in ~50% of cases. Early diagnosis has been improved by ultrasonography, with a consequent decrease in morbidity and mortality. During the last decade, in an attempt to avoid hysterectomy and preserve fertility, more conservative surgical approaches were developed including intra-cervical balloon tamponade after cervical curettage, cervical cerclage, hypogastric iliac artery ligation, arterial embolization under angiographic curettage, local prostaglandin injection and hysteroscopic resection.<sup>2-11</sup> On the other hand surgical techniques has the risk of abundant bleeding and medical treatment methods using methotrexate (MTX), actinomycin-D and etoposide have recently been developed.<sup>12-17</sup> In this report, we present a conservative approach using treatment with MTX for cervical pregnancy.

## Case report

A 35-year-old woman, gravida 2, abortion 1 was admitted to our department at 6 weeks gestation for the first antenatal

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*Submitted for Publication:* 05.04.2008

*Accepted for Publication:* 28.04.2008

visit. Her medical history was remarkable, with previous intrauterine procedure for 12 weeks intrauterine ex fetuse gestation and she uses levothyroxine for hypothyroidism. Vital signs were stable, and the abdomen was soft and not tender. Pelvic examination revealed a barrel-shape uterine cervix with minimal bright bleeding protruding through a closed external os. The uterus was slightly enlarged and had no adnexal masses. Transabdominal and transvaginal ultrasound examinations (Aloka SSD prosound 5500, Tokyo, Japan, 5 MHz) confirmed the presence of a cervical pregnancy with fetal pole and fetal cardiac activity (Figure 1). Quantitative beta-human chorionic gonadotrophin ( $\beta$ HCG) concentration was 37378 mIU/ml on admission.



*Figure 1: Cervical pregnancy with fetal pole and fetal cardiac activity*

In an attempt to preserve fertility, we offered the patient conservative management with intramuscular (im) MTX. The potential risks and alternative methods of treatment were explained to her, and written informed consent was obtained. The most commonly used treatment regimen in our department was applied. This consisted of im MTX 1 mg/kg and folic acid 0.1 mg/kg given alternately every other day for 4

days. The patient's complete blood count (CBC) with hemogram (Hb) =12,8, white blood cell (WBC)=9110, platelet (plt)=247.000 and liver function tests ALT/AST=26/22 mIU/ml were normal at admission. On the first day of MTX therapy, disappearance of fetal cardiac activity was determined with ultrasound examination. On the fifth day of medical treatment, despite decreasing  $\beta$ HCG value (24283 mIU/ml) sudden profuse vaginal bleeding has been occurred. On the basis of the patient's haemodynamically stable state and cessation of vaginal bleeding after two days, we decided to follow up the patient conservatively. In laboratory findings Hb(11,6) was decreased a little and liver enzymes were increased (ALT/AST=37/31). There were 2x2cm gestation material at cervix on speculum examination and ultrasound imaging showed 41x21mm gestation sac with CRL=10mm ex fetus. One more dose of MTX was repeated. During expectant management, vaginal spotting has been continued and liver enzymes were increased (ALT/AST=91/41). Because of impaired liver function, MTX therapy has not been repeated. On the tenth day of MTX treatment  $\beta$ HCG level was 12362 mIU/ml, on the 13th day  $\beta$ HCG level was significantly decreased to 4183mIU/ml and cervical gestation sac was decreased to 12x12mm diameters. One week later  $\beta$ HCG level was regressed to 363 mIU/ml, gestation sac was measured 5x5mm diameters and the amount of vaginal spotting has been diminished. The  $\beta$ HCG concentration continued to drop to 68 mIU/ml level and gestation sac was disappeared two weeks later. With the commencement of menstruation, the pelvic sonography was evaluated as normal.

## Discussion

Cervical pregnancy is a rare form of ectopic pregnancy, although its prevalence may be increased in patients undergoing in vitro fertilization.<sup>18</sup> With the introduction of high resolution ultrasound and sensitive serum  $\beta$ HCG assay, cervical pregnancy is diagnosed much earlier.

There are two main treatment options for cervical pregnancy when fertility is desired: surgical and pharmacological. The different methods described<sup>18</sup> include cervical cerclage, intracervical balloon tamponade of the cervix, vaginal packing, local haemostatic sutures, curettage followed by local prostaglandin instillation,<sup>19</sup> ligation of the descending branches of the uterine arteries, and bilateral hypogastric artery ligation. Since the early 1980s there have been many reports of the successful and unsuccessful use of chemotherapy; MTX has been variously administered by the im, intravenous, intracervical and intra-amniotic routes.<sup>20,21</sup> The presence of fetal cardiac activity or advanced gestational age has not influence to the success rate of treatment.<sup>22</sup>

In our case, in an attempt to preserve fertility, we chose a conservative approach. We suggest that MTX, which seems

by far the best choice for treatment of cervical pregnancies, should be offered first by the im route, by the routine protocol most commonly used by the department, which is considered simple and safe. If on follow-up evaluation,  $\beta$ HCG concentrations do not decrease (15% from baseline) or persistent fetal cardiac activity is observed, direct intra-arterial MTX should be instituted.<sup>23,24</sup>

Massive hemorrhage is the serious complication of the cervical pregnancy and reported the incidence 29,1% at the time of admission to the hospital.<sup>18</sup> Spotting or mild bleeding rate was seen only 20,2% of patients. The patient had mild bleeding when she admits to the hospital and the bleeding was continued as spotting after MTX treatment.

The adverse effect of MTX administration includes bone marrow depression, nausea, vomiting, diarrhoea, oral ulcers, stomatitis and high doses can cause significant myeloid suppression, acute and chronic hepatotoxicity, pulmonary fibrosis<sup>25,26</sup> Local treatment was chosen to avoid the adverse effects of the systemic MTX administration. Intra-cervical or intra-amniotic administration were used successfully to treat the cervical pregnancy recently.<sup>14,20</sup>

In previous reports, a gestational age of >9 weeks, serum  $\beta$ HCG concentration of >10000 mIU/ml, a crown-rump length>10mm and embryonic cardiac activity were associated with unsatisfactory results of MTX treatment.<sup>18</sup> However Kim et al. reported that the fetal heart activity and the size of gestation sac did not affect the treatment efficacy of medical or surgical treatment<sup>22</sup>

In conclusion, early diagnosis and appropriate MTX regimen could contribute to successful treatment with preservation of the uterus and future reproductive ability.

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## Servikal Gebeliğin Metotreksat Uygulamasıyla Başarılı Tedavisi

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İntramüsküler metotreksat tedavisi ile başarılı şekilde tedavi edilen servikal gebelik olgusu sunulmaktadır. Çalışmamız göstermektedir ki, fertilité korunması amaçlanıyorsa ve hastanın kliniği uygun ise servikal gebelikte medikal tedavi uygulanabilir

**Anahtar Kelimeler:** Servikal gebelik, Metotreksat, Fertilité koruma

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