

Successful Treatment of a Cervical Pregnancy by Single Dose Methotrexate and Vaginal Misoprostol

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Abstract

Cervical pregnancy is an extremely rare form of the ectopic pregnancy. The aim of this case report is to show that single dose methotrexate and vaginal misoprostol could be an alternative therapy to surgery.

A 34-year-old, gravida 3, parity 3, patient who had vaginal spotting and 15-day menstrual delay according to her last menstrual cycle, was admitted to our hospital. The serum β -hCG level of the patient was 23 000 mIU/ml and transvaginal ultrasound revealed a vacancy in the uterine cavity and the localization of the gestational sac in the cervical canal. An embryo with CRL 6.6 mm, with heart-beat, consistent with 6-week and 3-day pregnancy was present. The patient was given a single dose of 50 mg/m² methotrexate (85 mg). Four hundred μ g misoprostol was administered to the posterior fornix of the vagina on the second day of the methotrexate therapy, repeating dose of misoprostol was given on the third day as no cervical changes were detected, heart rates were lost on the fifth day and finally abortion was achieved on the eighth day. No major bleeding occurred and no surgical intervention needed. The patient then was followed up by sonographic examinations and serum β -hCG measurements.

This ectopic cervical pregnancy case was treated successfully with a single dose methotrexate and misoprostol. In selected cases single dose methotrexate and misoprostol may become a useful alternative to surgical intervention for the management of viable cervical pregnancy.

Keywords: cervical pregnancy, conservative treatment, methotrexate, misoprostol

Özet

Tek Doz Metotreksat ve Vajinal Mizoprostol ile Servikal Bir Gebeliğin Başarılı Tedavisi

Servikal ektopik gebelik, ektopik gebeliklerin en nadir görülen tipidir. Bu vaka sunumumuzun amacı, servikal ektopik gebeliğin tedavisinde tek doz metotreksat ve vajinal mizoprostolün cerrahi tedaviye alternatif olabileceğini tartışmaktır.

Otuz dört yaşında gravida 3, parite 3 olan hasta, son adet tarihine göre 15 günlük adet gecikmesi ve vajinal lekelenme şikâyeti ile polikliniğimize başvurdu. β -hCG değeri 23 000 mIU/ml olan hastaya yapılan transvajinal ultrasonografide uterin kavitenin boş olduğu ve gebelik kesesinin servikal kanala yerleşmiş olduğu görüldü. Kese içinde CRL 6.6 mm, fetal kardiyak aktivitesi olan 6 hafta 3 gün ile uyumlu tek embriyo mevcuttu. Hastaya tek doz 50 mg/m²lik metotreksat (85 mg) verildi. Metotreksat tedavisinden sonraki ikinci günde, vajen arka forniksine 400 μ g/gün mizoprostol yerleştirildi; servikal değişiklik olmayınca üçüncü gün mizoprostol dozu tekrarlandı, beşinci günde fetal kalp atımı kayboldu, sekizinci günde düşük gerçekleşti. Ciddi bir kanama oluşmadı ve cerrahi girişim gerekmedi. Hasta ultrasonografi ve serum β -hCG ölçümleri ile takip edildi. Vakamızda, servikal gebelik konservatif yolla başarılı olarak tedavi edilmiştir. Seçilmiş uygun canlı servikal gebelik vakalarında metotreksat ve mizoprostol cerrahi tedaviye iyi bir alternatif olabilir.

Anahtar sözcükler: servikal gebelik, konservatif tedavi, metotreksat, mizoprostol

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Introduction

Cervical pregnancy is a rare event that exists approximately in 1% of all the ectopic pregnancies and 1 to 2400 in 50 000 pregnancies overall. It is a life threatening state because of the uncontrollable massive hemorrhage from the cervical vessels (1). The traditional mode of treatment for cervical pregnancy is hysterectomy, but this treatment is an extremely radical approach especially for young patients. In patients who want to maintain their fertility, a more conservative treatment is highly desirable.

Recently, new conservative treatment options have been suggested to preserve fertility. This includes methotrexate with or without additional therapeutic procedures, such as dilatation and curettage followed by intracervical balloon blocking, uterine artery embolisation or ligation and cervicotomy. Unfortunately, there is no agreement on a definitive choice of treatment of these patients because of the rarity of this entity. Among the conservative treatment regimens, methotrexate is widely applied for the management of selected cases, but additional surgical methods which include dilatation and curettage or vacuum curettage are often needed to remove the gestational tissue which can cause dangerous bleeding.

We report a real cervical pregnancy case that was successfully treated with a single dose of systemic methotrexate and to intravaginal misoprostol without need for any surgical intervention.

Case Report

A 34-year-old woman, gravida 3, parity 3, was admitted to the gynecology department with a history of minimal vaginal bleeding and 15-day amenorrhoea. Physical examination of the patient was normal. She was bleeding minimally and the bleeding was confirmed to originate from the cervical canal by the speculum examination. On pelvic palpation, the cervix was distended, the external os was not dilated. Quantitative (β -hCG) level was 23 000 mIU/ml on admission. According to her last menstrual period, she was approximately 6 weeks pregnant. On transvaginal sonography uterine cavity was empty and endometrial thickness was measured 13 mm. A gestational sac containing a live embryo was observed in the cervical canal (Figure 1). Crown-rump length of the embryo was 6.6 mm, consistent with 6 weeks, 3 days of pregnancy.

Treatment modes, with their potential risks were discussed with the patient and her husband. Although conservative treatment of cervical pregnancy with methotrexate is highly successful, in some cases with presence of embryonic cardiac activity and β -hCG concentration of >10 000 mIU/ml, as in this one, the success rate decreases and additional surgical interventions become necessary. As the patient was young and desired to preserve her fertility, conservative treatment with a single dose of systemic methotrexate and intravaginal misoprostol was offered. After obtaining written consent, upon being informed, from the patient and her husband, the



Figure 1. Complete longitudinal vaginal septum

patient was given a single dose of 50 mg/m² of methotrexate (85 mg). Complete blood count, liver function tests, measurement of blood urea nitrogen and creatinin levels were made before the administration of methotrexate. Two days after the methotrexate treatment, 400 μ g/day misoprostol was administered to the posterior fornix of the vagina. Follow up sonographic examinations and serum β -hCG measurements were performed every two days. Twenty four hours after the initial dose, upon detection of no change on the vaginal sonogram and in the cervix, intravaginal misoprostol (400 μ g/day) was repeated and cervical dilatation and vaginal bleeding was achieved. Since a brownish discharge had occurred, oral cefuroxime and metronidazole was initiated. On the 5th day of methotrexate therapy, speculum examination revealed moderate bleeding from the cervix, and the external os was 2 cm dilated. Furthermore, ultrasound examination revealed fetal demise and regression of the gestational sac. On the 8th day after the initial dose of methotrexate, gestational sac was aborted without need for any surgical intervention. Ultrasonographic evaluation confirmed that abortion was complete. No remarkable bleeding and drug side effects were observed during this interval. The patient was discharged after a week without any complications. She was followed up as an outpatient by periodic ultrasonographic examinations and serial measurements of β -hCG. At the first control a week after discharge, there was minimal vaginal bleeding; serum β -hCG level had dropped to 700 mIU/ml and transvaginal ultrasonography showed a 12x22 mm heterogeneous echogenic area (placental tissue) in the cervix. Serum β -hCG titre dropped to the normal non-pregnancy range in 6 weeks. Trophoblastic tissue disappeared 12 weeks after the methotrexate treatment.

Discussion

Cervical pregnancy has the highest mortality rate among the ectopic pregnancies. If not detected early, profuse hemorrhage may occur from the cervical vessels and may necessitate an hysterectomy (2).

In selected cases medical management of cervical pregnancy is a good alternative to surgical management. The most commonly preferred medical agent is methotrexate. Its effect on pregnancy tissue appears to be predominantly on the trophoblast and leaves the secretion of progesterone by the corpus luteum intact. Thus, death of the embryo, destruction of the trophoblast and decline in hCG and placental progesterone may take some days or weeks to occur. The fall in progesterone concentration results in increased uterine contractility, bleeding and eventual expulsion of the conceptus (3). Unfortunately, there is no consensus in methotrexate treatment. Methotrexate may be used systemically, locally or combined. Hung (4) claimed that patients undergoing systemic administration of methotrexate tended to respond satisfactorily, compared with local injection or a combination of both methods, although the difference was not statistically significant. Also methotrexate is associated with many unpleasant side effects such as bone marrow suppression, liver function abnormalities, stomatitis and nausea. A small dose and duration of therapy for ectopic pregnancy limit the side effects. In our case, we preferred single dose regimen to multidose regimen in order to exclude any kind of side effects.

Misoprostol is a prostaglandin E₁ analogue and it has been widely used in obstetrics for pregnancy termination. Although, misoprostol is meant for oral use, vaginal administration of the tablets is often used and found more effective in stimulating uterine contractility and cervical ripening. The overall success rate of misoprostol has been 85%, with water added to the tablets before using for treatment. This was 94.4% for gestation of ≤ 7 weeks and only 77.4% for gestation of 7 to 9 weeks. Easy administration and minor side effects are the other advantages of misoprostol use (3).

Methotrexate treatment success rate in cervical pregnancy is reported to be 91%, but in some cases, initial methotrexate treatment fails and additional interventions are required, especially if failed results are associated with presence of embryonic cardiac activity, β -hCG concentration of $>10\,000$ mIU/ml, a gestational age of >9 weeks and a crown-rump length >10 mm (4). In our case, two days after the methotrexate treatment, 400 μ g/day misoprostol was administered vaginally to decrease the probability of failure in the initial methotrexate treatment (β -hCG concentration was $>10\,000$ mIU/ml and embryonic cardiac activity was present).

Methotrexate has been used in combination with misoprostol for termination of early pregnancies for a long time. Methotrexate and misoprostol combination therapy rema-

ins an effective method of termination up to day 63 of pregnancy, carries little risk to women, and with a 98% success rate (5). These results encourage us to use this combination as an alternative procedure for cervical ectopic pregnancy termination.

Rosenman (6) has used systemic methotrexate at a dose of 1 mg per kg and four days later added 800 μ g of vaginal misoprostol successfully. Although, our methotrexate regimen and misoprostol dose were different from their treatment, we have achieved successfully the termination of the cervical pregnancy. Mendilcioğlu (7) has used misoprostol intracervically successfully to terminate a non-viable cervical pregnancy. Probably non-viability of the embryo improves the success rate and decreases the need for a surgical intervention. In 1994, Dall (8) reported the use of prostaglandin both systemically and intraamniotically, in a patient with cervical pregnancy. Despite combined with simultaneous dilatation and curettage, intractable hemorrhage necessitated an emergent hysterectomy.

As cervical pregnancy is so rare and experience is limited with case reports and metaanalyses only, we report this case to encourage further future studies addressing the efficacy of methotrexate with misoprostol.

There is no consensus on the most appropriate treatment for cervical pregnancy. From our point of view, single dose systemic methotrexate injection with vaginal misoprostol combination treatment is a successful and safe alternative to surgical interventions for the management of cervical pregnancies with live embryo.

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