






## Case Report

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# An Algorithm for Treatment of Cervical Pregnancy: Report of a Series of Eight Patients

Azam Tarafdari , Sedigheh Borna , Sheida Janatrostami , Fatemeh Farajzadeh Vajari\* *Department of Obstetrics and Gynecology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.*

**Citation:** Tarafdari A, Borna S, Janatrostami S, Farajzadeh Vajari F. An Algorithm for Treatment of Cervical Pregnancy: Report of a Series of Eight Patients. *Case Reports in Clinical Practice*. 2020; 5(4):101-105.

**Running Title:** Successful Treatment of Cervical Pregnancy

**Article info:****Received:** 08 October 2020**Revised:** 22 November 2020**Accepted:** 18 December 2020**Keywords:**

Cervical pregnancy; Systemic methotrexate; Uterine artery embolization

**ABSTRACT**

Being considered as an important life-threatening condition, Cervical Pregnancy (CP) is defined as the implantation and growth of the gestational sac in the endocervical canal. Due to high maternal mortality and morbidity expectant management is not recommended. There is no definite treatment for this complication. During this case series study, we used an algorithm for CP treatment according to gestational age, presence of fetal heart activity, hemodynamic stability, and patients desire for future fertility in 8 patients. We used a combination of several modalities such as fetal heart reduction, systemic methotrexate, and uterine artery embolization to successfully treat all of them. Reproductivity ability of all patients has been reserved and 3 pregnancies including 2 terms and 1 preterm occurred during the follow-up period.

**Introduction**

**E**ctopic Cervical Pregnancy (CP) is a rare maternal event and accounts for less than 1% of all ectopic pregnancies [1]. No definite cause is determined for CP. Local pathologies can be predisposing factors and previous surgeries and artificial technologies have increased its preva-

lence, too. Painless vaginal bleeding or bleeding with lower abdominal pain are its common manifestations. Consequently, it is necessary to differentiate CP from an intrauterine pregnancy and, in particular, from an incomplete abortion [2, 3].

Transvaginal ultrasound findings besides physical examination are useful diagnostic methods to support de-

**\* Corresponding Author:****Fatemeh Farajzadeh Vajar, MD.****Address:** Department of Obstetrics and Gynecology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.**E-mail:** [fatameh\\_582003@yahoo.com](mailto:fatameh_582003@yahoo.com)

cision making and proper management. Imaging findings may illustrate regular gestational sac contour, with echogenic rim but without sliding sac sign, diagnostic for incomplete abortion, and a closed internal cervical os, which assist to confirm the diagnosis [4]. Though transvaginal sonography has significantly shown up its diagnostic process, management of CP depends on embryonic age, patients' stability, future reproduction state, and access to instrumentation and facilities. Considering the rarity of CP, we report data of patients treated according to our protocol to document a possible management plan for such cases.

### Patients and Methods

In a retrospective study, data of all patients with a final diagnosis of CP admitted to and treated at Valiasr Hospital from March 2015 to March 2019, were collected. The diagnosis was confirmed by transabdominal and transvaginal sonography. Ultrasonography criteria for diagnosis included defined gestational sac in the cervix, trophoblastic invasion to the cervix, and assessing endometrium and uterine body. The following data were collected: level of beta-human chorionic gonadotropin ( $\beta$ -hCG), gestational age and size of ectopic pregnancy, future pregnancy desire, and ultrasonography findings.

### Treatment protocol

Our protocol for CP was extracted from literature and had received the consensus of the department attending physicians and is directly a replication of the protocol we already reported for cesarean scar pregnancy. Accordingly, patients who had children and complete family planning were considered to undergo a hysterectomy. Patients with severe bleeding who were hemodynamically unstable were considered to receive interventional embolization of the uterine artery. In the instance of an alive fetus without severe bleeding, KCl injection to fetal heart was done and these patients and those without fetal cardiac activity received methotrexate (MTX) according to the level of  $\beta$ -hCG (Table 1). These later patients would undergo sonography again and take uterine artery embolization if placental vascularity was high and vaginal bleeding continued. At the end of admission, the patients were discharged and reminded about the alarming signs (i.e., bleeding, fever, and abdominal pain). They were followed by a weekly measurement of  $\beta$ -hCG levels until the  $\beta$ -hCG level reaches  $\leq 5$  mIU/mL when the absence of gestational products was confirmed by vaginal ultrasonography.

The following data were extracted for analysis as the surrogate indices for the success of the therapy: the time to reach the negative  $\beta$ -hCG level, time to normal mensuration, need to remove the remaining product, and future pregnancy.

### Results

Eight patients with CP, one after intrauterine insemination, and 7 with spontaneous pregnancies, were included. The demographic data are summarized in Table 2. No hysterectomy was planned. Four patients (50%) had fetal cardiac activity, for whom 3 mL KCl 15% was injected into a fetus's heart with a guide of vaginal ultrasonography under sedation in the operating room. The next day, ultrasonography was done to confirm the absence of fetal cardiac activity when a decision or MTX injection was made according to the  $\beta$ -hCG level. Among 4 cases in need of reduction, one mother was primigravida and had twin pregnancy with one fetus in the fundus and the other one was CP. Fetal cardiac KCl injection was done for CP. MTX injection was not done for this case. One week after the reduction of CP, the other pregnancy was aborted too. Seven patients received MTX (Table 3).

All CPs who underwent fetal reduction were hypervascular in ultrasonography evaluation. Two cases (25%) experienced diminished vascularity following methotrexate injection. But 2 other cases received uterine artery embolization (UAE) too because of the hypervascular placenta and continuous vaginal bleeding.

The patients had normal menstruation after 2.4 0.3 months. The average time to reach negative  $\beta$ -hCG ( $< 5$  mIU/mL) was 6.01 weeks and the mean time for gestational product disappearance was  $2.6 \pm 0.2$  weeks. Primary treatment was successful and no suction and curettage or hysterectomy was subsequently needed. No blood transfusion was needed. Also, infection or metritis was not seen in any patient. In the follow-up period (range 12-50 months), two patients had successful term pregnancy, and another patient presented with premature labor which happened due to cervical insufficiency at 24 weeks of gestation.

### Discussion

We presented an efficient and safe non-surgical approach for the management of CP. It has been already documented that reproducibility can be preserved in more patients with less invasive treatments. Local and systemic MTX injection is one of the acceptable thera-

**Table 1.** The method for intravenous methotrexate (MTX) injection according to  $\beta$ -hCG level

B-hCG (mIU/mL)	MTX Injection(s)
<1000	No MTX injection
1000-5000	Single dose 50 mg/m <sup>2</sup>
5000- 8000	Double dose 50 mg/m <sup>2</sup> on days 1 and 4
8000	Multiple dose on days 1, 3, 5, and 7 and folinic acid 1 mg/kg on days 2, 4, 6, and 8



**Table 2.** Patients' demographic characteristics (N=8)

Health Characteristics	Mean $\pm$ SD / No. (%)
Age (y)	32 $\pm$ 7.71
BMI (kg/m <sup>2</sup> )	26.42 $\pm$ 4.92
Married time (y)	7.4 $\pm$ 7.3
Middle gravidity	2 (1-2.5)
Middle parity	0 (0-1)
Abortion	0 (0-1)
Interval of caesarian section (y)	10 (10-10)
Pervious myomectomy	0 (0%)
Previous caesarian section	3 (37.5%)
Previous curettage (no.)	2 (25%)



pies applied worldwide [5]. In this way, the uterus can be saved in 80% of cases [2]. The inclusion criteria to select patients for medical treatment was limited to hemodynamically stable patients [6-8].

Single or multiple dose injections are recommended in the primary stages of pregnancy with minimal side effects [9]. In contrast to available protocols for tubal ectopic pregnancy where certain stable patients could be best treated by MTX as first-line therapy, for CP, there are no accepted criteria for the selection of medical versus surgical treatments [10]. Furthermore, CP in advanced gestational ages with cardiac activity demands KCl injection to fetal heart in the operating room to minimize bleeding risks [11]. Severe vaginal bleeding may require UAE, and surgery, dilation, and curettage or hysterectomy are the last choices [12]. All patients in our study wanted to save their fertility and our protocols satisfied them. UAE is considered a safe method with certain con-

sequences, including transient claudication of buttocks [13] that we did not record in the patients received UAE.

To solve the problem, Kim et al. reported their experiences and described a size 26 Foley catheter usage to stop bleeding with uterine drainage by inflated balloon in CPs [14]. Wang et al. treated 16 CPs with embolization and curettage and their patients had 3 successful pregnancies [15]. Curettage follows severe vaginal bleeding which becomes a major obstacle for the patient and physician. In contrast, Murji et al. studied 27 patients with CP when 3 patients had severe vaginal bleeding. However, they treated patients conservatively in all cases to show the efficacy of MTX alone or combined approaches [16].

The results of the current study support the conclusion of Murji et al. to highlight the safety and efficacy of conservative medical therapy. Similarly, Varma used systemic MTX with KCl injection in 24 patients and only 4 patients needed extra interventions to confirm the efficacy of less-invasive

**Table 3.** Therapy-related characteristics of patients with cervical pregnancy (N=8)

Therapy Data	Mean±SD / No. (%)
Gestational age (wk)	7.21±0.94
Blood transfusion	0 (0%)
Initial β HCG (mIU /mL)	30377.0±35381.4
Absence pregnancy	5 (62%)
Successful term pregnancy	2 (25%)
Unsuccessful term pregnancy	1 (12.5%)
KCl injection	4 (50%)
Single doze MTX	2 (25%)
Double dose MTX	2 (25%)
Multi doze MTX	3 (37.5%)
Hysterectomy	0 (0%)
UAE	2 (25%)

UAE: uterine artery embolization; MTX: methotrexate.



management [17]. Alternatively, Spiros evaluated patients after MTX therapy with β-hCG level every 3 days and ultrasound assessment. When the β-hCG level dropped, they did curettage and recommended this approach for CP [18]. We illustrated that after MTX injection, no further invasive procedure was necessary for complete treatment.

The protocol we employed was acceptable because none of the patients underwent hysterectomy nor showed infections and they experienced normal menstruation within 2.4 months (on average) in the follow-up. Out of 8 patients, 2 had following successful term pregnancy and 1 preterm labor.

Conservative therapy employing MTX combined with fetal reduction and UAE, when necessary, is a good choice in CP. Interestingly, we used the same approach with rather similar results for scar ectopic pregnancies. We recommend considering parameters such as clinical presentation, initial β-hCG level, fetal heart activity, gestational age, and ultrasound findings to adjust available managements.

## Ethical Considerations

### Compliance with ethical guidelines

This study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of

Helsinki and all subsequent revisions. The participants written informed consent form was collected before the study.

### Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

### Conflict of interest

The authors declared no conflict of interest.

### Acknowledgements

The authors would like to thank the patients as well as the staff of Department of Obstetrics and Gynecology, Imam Khomeini Hospital Complex for all their help.

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