## CASE REPORT

# Successful Conservative Treatment for Large Cervical Ectopic Pregnancy

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#### ABSTRACT

A rare case of cervical ectopic pregnancy presented with vaginal bleeding. Pelvic examination revealed large soft bluish mass at the posterior lip of the cervix. Transvaginal ultrasound showed a cervical mass with a gestational sac and 7-mm fetal echo without cardiac motion. Initial serum betahuman chorionic gonadotropin (hCG) was 29,489 mIU/ml. A two-dose regimen of methotrexate was intramuscularly administered. Bilateral uterine artery embolization was performed on day 14 due to heavy bleeding. One week later, sharp curettage at the cervical implantation site was carried out again because of re-massive bleeding. After discharge, serum beta-hCG levels were normal on day 45. Pathological study confirmed the clinical diagnosis of cervical ectopic pregnancy.

Keywords: cervical ectopic pregnancy, methotrexate, uterine artery embolization.

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Received: 22 February 2019, Revised: 29 July 2019, Accepted: 31 July 2019

## Introduction

Cervical ectopic pregnancy (CEP) is a rare type of ectopic pregnancy<sup>(1)</sup>. The incidence of CEP is 1 per 10,000 deliveries (less than 0.1% of all ectopic pregnancies)<sup>(2)</sup>. The etiology of CEP remains unknown. Risk factors for CEP include previous ectopic pregnancy, previous cesarean delivery, previous uterine or cervical surgery, in vitro fertilization, history of pelvic inflammatory diseases, smoking, previous pelvic surgery, intrauterine device use, and anatomic anomalies of the genital tract<sup>(3)</sup>. As CEP can cause catastrophic hemorrhage, early diagnosis and timely management are of the utmost importance. Most of CEP cases are treated by hysterectomy<sup>(2)</sup>.

Methotrexate (MTX), a folinic acid antagonist, is an effective medical treatment for ectopic pregnancy with success rate 90% in properly selected cases, mostly tubal pregnancy<sup>(4-6)</sup>. It can be administered via either systemic or local injection. There are various single-dose (one-dose and two-dose) and multiple-dose systemic MTX regimens that are prescribed<sup>(4, 5, 7)</sup>. However, there is no standard regimen of systemic MTX for CEP. Uterine artery embolization (UAE) is common carried out concurrently in case of severe hemorrhage<sup>(8, 9)</sup>. Curettage at the implantation site and vaginal packing has been reported as a successful conservative treatment for cervical pregnancy with MTX in low-resource settings<sup>(10)</sup>. Herein, we report a case of CEP that was treated with MTX, UAE, and curettage in order to preserve the uterus.

## **Case presentation**

A 36-year-old woman, parity 2, was referred from a community hospital to our hospital due to bleeding per vagina for 1 day without pelvic pain, nausea, or vomiting. Her underlying disease was hypertension. She was taking combined oral contraceptive pills irregularly and denied having missed her period. Her vital signs were normal. Her abdomen was soft without any abnormal masses or tenderness on palpation. Pelvic examination revealed an 8-cm, soft, dark bluish mass at the posterior lip of the cervix with minimal bleeding. A urine pregnancy test was positive. Transvaginal ultrasound showed a cervical mass 4.9 x 4.5 cm in diameter with a gestational sac and fetal echo. The uterine cavity was empty. There was a 7-mm fetal pole without cardiac motion that appeared to be at corresponded with 7+ weeks of gestation (Fig. 1). No fluid was detected in the cul-de-sac. The patient's initial serum beta-human chorionic gonadotropin (hCG) was 29,489 mIU/ml. A clinical diagnosis of CEP was made.



**Fig. 1.** Transvaginal ultrasonography revealed an abnormal mass with a gestational sac and fetal echo occupying the posterior lip of cervix.

A two-dose regimen of MTX at 50 mg/m<sup>2</sup> was administered intramuscularly on days 1, 4, 7, and 11. No adverse effects were observed during hospitalization. The patient's serum beta-hCG declined to 5,298 on day 14 after treatment, but she developed heavy vaginal bleeding requiring a transfusion of 4 units of packed red cells. Bilateral UAE was performed by the interventional radiologist and the vaginal bleeding dramatically decreased after the procedure.

One week later, the patient experienced a recurrent episode of massive vaginal bleeding. Pelvic examination revealed a 5-cm soft bluish mass at the

posterior lip of the cervix with bleeding from the mass site. The active cervical bleeding was successfully controlled by sharp curettage at the cervical implantation site followed by vaginal packing within the first 24 hours after the procedure. The patient did not experience any massive vaginal bleeding thereafter.

A weekly serum beta-hCG blood test was administered, which yielded a negative result on day 45 of MTX injection. Pelvic examination on follow-up day 45 revealed a normal cervical contour and proper healing (Fig. 2). Pathological examination of the curettage specimens revealed the presence of chorionic



Fig. 2. Per vaginal examination revealed a normal cervical contour after treatment.

### Discussion

We reported a rare case of cervical ectopic pregnancy. The most common presentation is painless vaginal bleeding with abnormal cervical masses or an enlarged cervix. In this case, the patient denied having missed her period, but was taking oral contraceptive pills irregularly.

The diagnosis of CEP has to be made based on physical examination and pelvic ultrasound. Ultrasound diagnostic criteria for CEP include an empty uterus, the gestational sac being located below the level of the internal os, a barrel-shaped cervix, and absence of sliding signs<sup>(3)</sup>. In our case, physical examination revealed a large cervical mass. In addition, transvaginal ultrasound showed a gestational sac with a yolk sac and fetal echo in the mass protruding from posterior lip of the cervix. The uterine cavity was also empty.

Hysterectomy is generally considered a mainstay treatment in cases of uncontrolled severe hemorrhage. Conservative treatment has become increasingly successful in cases of CEP due to early diagnosis being more common, technological advances, and new medications. In cases of early diagnosis, treatment with MTX, which inhibits DNA synthesis and cell reproduction, may be optional<sup>(5,6)</sup>. In this case, a total of four doses of a two-dose regimen of MTX were administered rather than a multiple-dose regimen as in other studies<sup>(10,11)</sup>. A two-dose regimen of 50 mg/m<sup>2</sup> of intramuscular

methotrexate was administered on days 0 and 4. Additional doses of methotrexate were administered on day 7 and/or day 11 if beta-hCG levels did not decrease by 15% during the follow-up period, as has been purposed by Barnhart et al<sup>(4)</sup> to lower the risk of potential side effects of a multiple-dose regimen whilst decreasing serum beta-hCG more rapidly than a single dose regimen.

In a systematic review of MTX treatment of ectopic pregnancy, Yang et al<sup>(11)</sup> reported comparable efficacy between multiple-dose and two-dose regimens but higher side effects in the multiple-dose regimen. In addition, folinic acid (leucovorin) rescue is not required for women treated with the single-dose protocol, even if multiple doses are administered<sup>(4)</sup>.

An intragestational sac or ultrasound-guided intracardiac injection of potassium chloride (KCL), mifepristone, and misoprostal to expulse the cervical gestational sac is another option for CEP treatment<sup>(12)</sup>. A report by Verma et al found that conservative treatment with systemic methotrexate and intragestational KCL sac injection was successful in 19 of 24 (79.2%) cases<sup>(12)</sup>. Interestingly, Osada et al<sup>(13)</sup> reported successful treatment of CEP by ultrasoundguided injection of absolute ethanol into the gestational sac.

UAE can be performed to control a life-threatening uterine hemorrhage in cases of severe postpartum

hemorrhage, morbid placenta adherence, and uterine fibroids<sup>(14)</sup>. In our case, UAE was performed to control massive bleeding from CEP. embolization with absorbable gelatin powder provides temporary obstruction of the blood vessels and allows for the development of collateral circulation. However, collateral flow may begin to develop within hours of the procedure. In our case, massive bleeding reoccurred one week after UAE, which might indicate the collateral flow formation in the vessels. There is no standard recommendation for the most appropriate timing to perform UAE, prophylactic procedure combined with MTX or only in a case that need to do an additional procedure such as uterine curettage or hysteroscopic resection of cervical pregnancy In our case, MTX was administered and UAE was performed later to prevent further massive bleeding. Unfortunately, curettage was subsequently required in order to control a recurrent episode of massive vaginal bleeding. These may be a large implantation size of cervical pregnancy. In contrast to a report written by Takeda et al, CEP was successfully treated with a combination of bilateral UAE and MTX<sup>(15)</sup>.

## Conclusion

Cervical ectopic pregnancy is a rare clinical entity that may result in hysterectomy if a lifethreatening hemorrhage occurs. Our report further demonstrates the benefit of methotrexate treatment in such cases. However, the large size of the cervical mass in this case caused severe bleeding, which required additional interventions including uterine artery embolization and rapid removal of the contraceptive product by sharp curettage at the implantation site to achieve adequate bleeding control.

## **Acknowledgments**

The authors would like to thank Dr. Dylan Southard for his English-language editing of this manuscript.

## Potential conflicts of interest

The authors declare no conflict of interest.

#### References

- Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year populationbased study of 1800 cases. Hum Reprod 2002;17:3224-30.
- Vela G, Tulandi T. Cervical pregnancy: the importance of early diagnosis and treatment. J Minim Invasive Gynecol 2007;14:481-4.
- Hosni MM, Herath RP, Mumtaz R. Diagnostic and therapeutic dilemmas of cervical ectopic pregnancy. Obstet Gynecol Surv 2014;69:261-76.
- Barnhart K, Hummel AC, Sammel MD, Menon S, Jain J, Chakhtoura N. Use of "2-dose" regimen of methotrexate to treat ectopic pregnancy. Fertil Steril 2007;87:250-6.
- Bachman EA, Barnhart K. Medical management of ectopic pregnancy: a comparison of regimens. Clin Obstet Gynecol 2012;55:440-7.
- Ozyuncu O, Tanacan A, Duru SA, Beksac MS. Methotrexate therapy for ectopic pregnancies: a tertiary center experience. Rev Bras Ginecol E Obstet 2018;40:680-5.
- Song T, Kim MK, Kim M-L, Jung YW, Yun BS, Seong SJ. Single-dose versus two-dose administration of methotrexate for the treatment of ectopic pregnancy: a randomized controlled trial. Hum Reprod 2016;31: 332-8.
- Hu J, Tao X, Yin L, Shi Y. Successful conservative treatment of cervical pregnancy with uterine artery embolization followed by curettage: a report of 19 cases. BJOG 2016;123:97-102.
- Lee C-H, Sacks J, Wong M, Cura M, Shaw C. Uterine artery embolization and potassium chloride injection for treatment of cervical pregnancy. J Vasc Interv Radiol 2017;28:1756-8.
- 10. Bettaiah R, Kamath SS. Effective hemostasis in cervical ectopic pregnancy with packing without hysterolaparoscopy or devascularization. J Minim Invasive Gynecol 2018;25:322-3.
- Yang C, Cai J, Geng Y, Gao Y. Multiple-dose and doubledose versus single-dose administration of methotrexate for the treatment of ectopic pregnancy: a systematic review and meta-analysis. Reprod Biomed Online 2017;34:383-91.
- Verma U, Goharkhay N. Conservative management of cervical ectopic pregnancy. Fertil Steril 2009;91:671-4.
- Osada H, Teramoto S, Kaijima H, Segawa T, Miyauchi O, Nagaishi M, et al. A novel treatment for cervical and cesarean section scar pregnancies by transvaginal injection of absolute ethanol to trophoblasts: efficacy in 19 Cases. J Minim Invasive Gynecol 2019;26:129-34.
- 14. Gonsalves M, Belli A. The role of interventional radiology in obstetric hemorrhage. Cardiovasc Intervent Radiol 2010; 33:887-95.

15. Takeda K, Mackay J, Watts S. Successful management of cervical ectopic pregnancy with bilateral uterine

artery embolization and methotrexate. Case Rep Emerg Med 2018;2018:9593824.