

CERVICAL PREGNANCY TREATED WITH SYSTEMIC METHOTREXATE ADMINISTRATION AND RESECTOSCOPY

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Cervical ectopic pregnancies are rare, but their incidence is increased in patients with previous cesarean deliveries, previous therapeutic abortions, Ascherman syndrome or *in vitro* fertilization [1]. Treatment is difficult, because dilatation and curettage of a cervical pregnancy frequently results in uncontrollable hemorrhage and the need for an emergency hysterectomy. Recent advances in high-resolution ultrasound and color Doppler have made the diagnosis of early cervical pregnancies easier, and have led to the development of several conservative approaches that preserve fertility. Several published reports have described the successful use of chemotherapy, such as methotrexate, in the management of cervical pregnancy. However, further intervention may be required following methotrexate treatment [2]. Here, we describe a case of a viable cervical pregnancy successfully treated with methotrexate administration and a resectoscopic procedure.

A woman, aged 34 years, gravida 4, para 2, abortus 1, presented at our emergency department with a 1-day history of lower abdominal pain and vaginal bleeding. She had previously received two cesarean sections, and her last menstrual period had occurred 7 weeks previously. She had visited her local gynecologist first and was transferred to our hospital because a viable cervical pregnancy was diagnosed.

Before examination, her vital signs were stable and her hemoglobin level was 12.8 mg/dL. The urine pregnancy test was positive. Pelvic examination revealed a small amount of bloody discharge protruding from the cervical os. Transabdominal sonography displayed an empty uterine cavity and a 20-mm gestational sac located in the cervical canal; this showed fetal cardiac activity. The color Doppler study demonstrated increased

flow in the posterior wall of the cervix (Figure 1). The initial serum human chorionic gonadotropin (hCG) level was 14,988 mIU/mL. A diagnosis of cervical ectopic pregnancy was made.

The patient was admitted and methods of pregnancy termination were discussed. She chose medical treatment by intramuscular injection of 50 mg of methotrexate. The patient's hematologic and biochemical parameters remained normal over the following 2 days after treatment. Her vaginal bleeding decreased to an unmeasurable level. She was discharged and scheduled for follow-up 1 week later.

The patient returned to our hospital with vaginal bleeding 3 days later. A sonographic scan showed an irregular gestational sac with no fetal heart activity. Color signals indicating peritrophoblastic flow were absent. Her hemoglobin level was 11.1 mg/dL, and her serum hCG concentration was 9,840 mIU/mL. She was readmitted. There was no active bleeding over the next 4 days, and the level of serum hCG decreased to 2,611 mIU/mL. We advised the patient that surgical intervention should be considered if the gestational sac was not expelled or if the size of the gestational mass remained unchanged over the next week. At 2 weeks after the first methotrexate therapy, the serum hCG level had continued to gradually decline, but intermittent vaginal bleeding was still present and the gestational mass in the cervical canal, which was unchanged in size, annoyed the patient. In view of the above problems, we arranged for hysteroscopic resection of the ectopic mass.

In the operating room, before dilatation of the cervix, sutures were placed at the 3 o'clock and 9 o'clock positions on the lateral sides of the cervix. A solution of 10 U of vasopressin diluted in 20 mL of saline was then injected intracervically at the 3 o'clock, 6 o'clock, 9 o'clock and 12 o'clock positions. The endocervical canal was dilated to 12 mm, and some tissue slid down. The hysteroscope was inserted into the cervix, and a small amount of residual tissue attached to the posterior wall of the cervix was identified and completely resected under direct visualization (Figure 2). We coagulated an



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Accepted: April 29, 2008

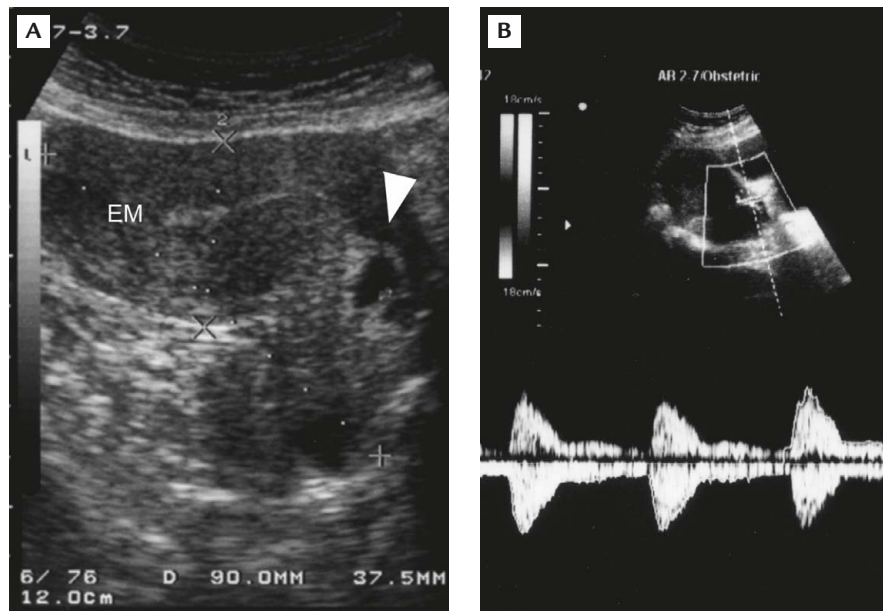


Figure 1. (A) The endometrial (EM) cavity is empty and a gestational sac with positive fetal heart beat is located in the endocervical canal. (B) Doppler sonography detects the vascular flow in the gestational sac in the posterior wall of cervix.

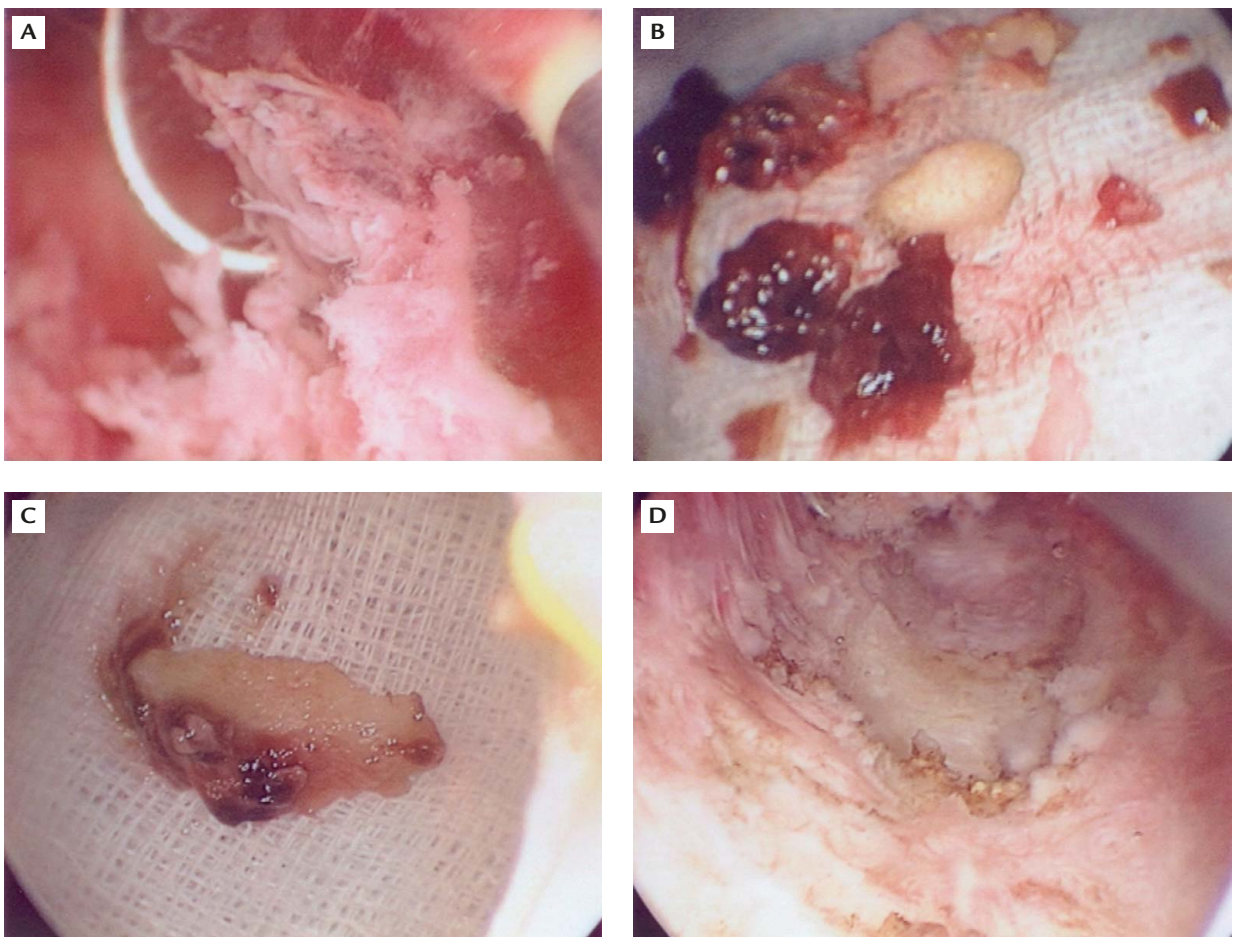


Figure 2. (A) The hysteroscopic finding after dilatation of the cervical canal is a small amount of gestational tissue on the posterior endocervical wall. (B) The residual gestational tissue is removed. (C) Some tissue adheres to the cervix. (D) The endocervix after electrocauterization.

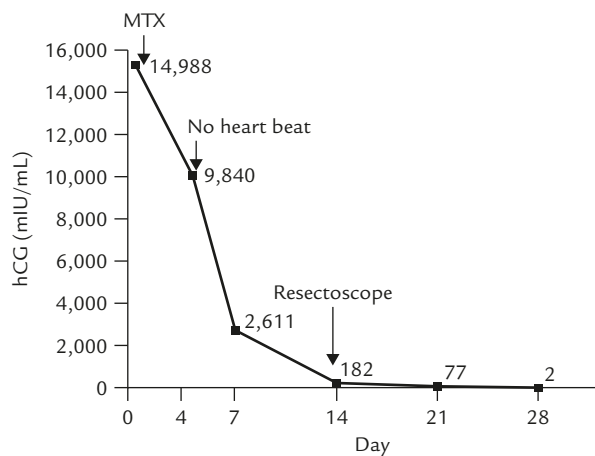


Figure 3. Changes in serum human chorionic gonadotropin (hCG) levels during and after methotrexate (MTX) treatment.

area of active bleeding using a loop electrode. The estimated blood loss during the operation was less than 10 mL. The procedure took approximately 30 minutes. The postoperative course was uneventful, and there was no more vaginal bleeding. The patient's serum hCG concentration was normal 14 days after the hysteroscopic resection (Figure 3). Her menstruation returned to normal 4 weeks after surgery.

The estimated incidence of a cervical pregnancy has been reported to range from 1/1,000 to 1/18,000 pregnancies [3]. Cervical pregnancy has traditionally been treated by hysterectomy because of profuse hemorrhage associated with curettage, due to presumed incomplete abortion. Alternative therapies that avoid the risk of uncontrollable hemorrhage and preserve fertility in women with cervical pregnancies are needed. These include cervical cerclage, cervical amputation, hypogastric artery ligation, cervical Foley tamponade, and uterine artery embolization [4]. In recent years, improved access to high-resolution ultrasound and rapid assays for serum hCG have made conservative treatments more feasible.

The application of the anti-metabolic drug, methotrexate, in the medical management of early ectopic pregnancy has been widely described, because it is both convenient to use and results in a good prognosis [2]. Several reports and case series since 1990 have cited success rates of more than 80% in selected cases using methotrexate therapy [1,4,5]. Nevertheless, cervical pregnancies presenting with serum hCG $\geq 10,000$ mIU/mL, gestational age ≥ 9 weeks, the presence of fetal heart beats or a fetal crown-rump length > 10 mm have been shown to be associated with a higher rate of primary methotrexate failure and may need additional interventions [6].

Methotrexate can be administered by two different routes. The systemic route has advantages over local

injection in terms of its simplicity, and is applicable in more patients [7]. The efficacies of high-dose and low-dose regimens are similar [6,8]. The main benefits associated with intra-amniotic injection are: (1) greater effectiveness, (2) a shorter treatment period, and (3) reduced dosage and toxicity compared with intramuscular administration [9]. However, this approach is technically more difficult than the parenteral route. There is a strong possibility of active bleeding following local injection, caused by rupture of the intra-amniotic membrane [10].

In this case, we initially opted for systemic (intramuscular) methotrexate administration to treat a cervical pregnancy of approximately 7 weeks' gestation. Although the patient's serum hCG levels were consistent with a satisfactory response to methotrexate and no fetal cardiac activity was detected, a sonographic scan revealed a persistent cervical mass. Common problems associated with methotrexate therapy, both local and systemic, include the inability to predict the occurrence of massive bleeding, the possibility of a slow resolution of the trophoblasts, and a time-consuming follow-up. Several studies have indicated that a persistent cervical mass should not be regarded as a treatment failure. In this case, the presence of diminished Doppler signs of peritrophoblastic flow and a decline in the serum hCG level reflected a therapeutic response [11,12]. Nonetheless, the size of the cervical pregnancy continued to increase after methotrexate treatment, possibly as a result of an inflammatory response, tissue swelling or internal hemorrhaging within the gestational sac. Furthermore, the pregnancy product may not be completely expelled. Despite a normal serum hCG concentration and resumption of the menstrual cycle, the mean period from initial methotrexate treatment until sonographic non-visualization of the cervical mass has been reported to be as long as 72 days [13]. Cervical pregnancy tissue retained in the cervix may serve as a culture medium for further infection [14]. Intractable bleeding is likely to occur owing to tissue sloughing and necrosis from the atonic cervix [6,11]. Surgical hemostasis and removal of the gestational mass should be considered to prevent these possibilities.

Operative hysteroscopy is superior to curettage, because it provides direct visualization of the ectopic location and its vascularity, which is helpful in achieving complete eradication and the accurate cauterization of any bleeding [15]. However, even minimal surgical methods, such as simple curettage or hysteroscopy, still carry a risk of uncontrolled bleeding, and the patient should be aware of the possible need for an emergency hysterectomy. Hysteroscopy also allows confirmation

of the diagnosis of cervical pregnancy [15,16]. We did not collect sufficient specimens in this case, and the pathology report described the presence of only a very small amount of necrotic tissue and endocervical tissue; but based on the sonographic and hysteroscopic findings, the diagnosis of cervical pregnancy was beyond question.

Some authors are hesitant to attempt removal of an ectopic mass after systemic methotrexate treatment, while others routinely attempt such a removal. Roussis et al demonstrated hysteroscopic resection of a cervical pregnancy for the first time in 1992 [17]. They performed resectoscopic surgery to remove the cervical mass at 40 days after systemic methotrexate administration. Before surgery, the serum hCG level was undetectable and decreased blood flow velocities were noted in the area of the gestational sac. Another patient with a 7-week viable cervical pregnancy underwent two courses of intramuscular methotrexate injections [18]. After the serum hCG level had declined and a dead embryo had been observed, operative hysteroscopy with ablation of the bleeding was carried out. These authors indicated that methotrexate therapy was able to induce effective regression of the viable cervical pregnancy, resulting in decreased blood loss during surgical intervention. Thus, complete resection via hysteroscopy was a safe procedure, and satisfactory hemostasis was easily achieved.

In order to avoid the side effects of methotrexate therapy, an alternative "one-stage" treatment using operative hysteroscopy has been reported. Ash and Farrell reported a 6-week viable cervical pregnancy that was successfully removed by hysteroscopic resection after ligation of the cervical branch of the uterine artery at the junction between the cervix and the vagina [15]. Jozwiak et al [19] described a woman with a 6-week cervical heterotopic pregnancy, who was treated by hysteroscopy alone, in order to preserve an intrauterine fetus. The woman delivered a healthy term baby. However, the safety of a simple hysteroscopic resection without preoperative blockage of the blood flow around the cervix remains unclear. Hysteroscopy may not be appropriate for more advanced gestations with better blood supplies. Kung et al reported six women with cervical pregnancies ranging from 6–9 weeks, who received resectoscopy immediately after laparoscopic uterine artery ligation [16]. The mean operative time was 119 minutes. Vilos et al described a procedure where hysteroscopic evacuation with transfemoral uterine artery embolization was successful for the treatment of a 10-week viable cervical pregnancy [20]. This patient initially presented with acute heavy bleeding. She had no active bleeding after embolization, and

serum hCG levels also decreased and fetal cardiac activity ceased. The authors then proceeded to hysteroscopic evacuation.

In our opinion, the laparoscopic procedure is too invasive, and angiographic embolization requires radiologic facilities with specialized instrumentation and expertise. Uterine artery occlusion is often performed to control massive bleeding in patients wishing to preserve their uterus or in patients with failed methotrexate treatment. However, potential harm to further fertility and pregnancy outcome has previously been demonstrated following uterine artery occlusion for the treatment of symptomatic myomas [21]. In addition, the possibility of rebleeding exists after blockage of the uterine arteries caused by deep invasion of gestational tissue into the cervical stroma, which remains alive after a short period of ischemia [22].

The most efficient treatment for cervical pregnancy remains uncertain. The incidence of cervical pregnancy is very low, making the evaluation of conservative methods by prospective randomized studies difficult. The choice of treatment is based on the patients' condition, their requirements, the risk factors, the availability of the various therapies, and the clinician's experience. We suggest that hysteroscopic resection should be performed following methotrexate treatment when: (1) there is a satisfactory decline in the serum hCG level, (2) the fetus is dead, (3) there is decreased peritrophoblastic flow, and (4) there is no active massive hemorrhage. In conclusion, systemic methotrexate administration combined with resectoscopic ablation can result in safe, successful remission of a cervical pregnancy, while maintaining satisfactory hemostasis.

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