

# Management of Cervical Ectopic Pregnancy with Small-Caliber Hysteroscopy

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## ABSTRACT

**Background and Objectives:** Cervical ectopic pregnancy is one of the rarest forms of ectopic pregnancy. We present a single center case series of 10 cases of cervical ectopic pregnancy, where 3 patients underwent small-caliber hysteroscopy as a single treatment method.

**Methods:** This was a retrospective study of women treated at our medical center with the diagnosis of cervical ectopic pregnancy from January 1, 2018 to December 31, 2020. Patient characteristics, medical history, obstetric history, diagnostic methods were collected. Small-caliber hysteroscopy treatment was performed in 3 patients and 7 patients underwent dilation and curettage (D&C).

**Results:** We identified 10 patients diagnosed with cervical ectopic pregnancy who were treated at our center. Ultrasonography was used to diagnose all cervical ectopic pregnancies. Three patients underwent small-caliber hysteroscopy as a single treatment option, while D&C was performed in 7 patients. Patients who underwent small-caliber hysteroscopy had a median gestational age at diagnosis of 7 weeks and initial  $\beta$ HCG < 10,000 mIU/

mL. These patients had shorter hospital stay and a lower estimated blood loss than patients who underwent D&C.

**Conclusions:** In our experience, small-caliber hysteroscopy is a safe and effective single treatment option for cervical ectopic pregnancy, but requires a skilled and experienced gynecologist.

**Key Words:** Cervical ectopic pregnancy, Ectopic pregnancy, Hysteroscopy, Small-caliber hysteroscopy, Ultrasonography.

## INTRODUCTION

Cervical ectopic pregnancy (CEP) is reportedly the rarest form of ectopic pregnancy. While nontubal pregnancies account for less than 10% of all ectopic pregnancies, implantation of an embryo inside the cervical canal occurs in less than 1% of all ectopic pregnancies.<sup>1</sup> The incidence of CEP ranges between 1 in 1,000 and 1 in 18,000 of all pregnancies.<sup>2,3</sup> Due to the lack of universally accepted guidelines for diagnosing and managing CEP, there is a discrepancy in the reported incidence. Even though the exact pathophysiology of CEP remains unknown, some of the major risk factors are well-documented: previous dilation and curettage, previous cesarean section delivery, surgical procedures for cervical pathology, and assisted reproductive technologies (ART).<sup>1,4</sup> Published reports suggest a rising percentage of CEP in recent years due to increasing rates of pregnancies conceived by ART.<sup>1</sup>

Traditionally, cervical ectopic pregnancy was mainly treated surgically by hysterectomy.<sup>5</sup> Advances in technology now provide an early diagnosis of CEP, allowing for conservative medical and minimally invasive surgical procedures.<sup>2,5</sup>

We present our experience of 3 patients with CEP treated at a single center with small-caliber hysteroscopy as a single treatment method.

## METHODOLOGY

We reviewed medical records of patients treated from January 1, 2018 to December 31, 2020, with the diagnosis

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Informed consent: Dr. Rastko Maglic declares that written informed consent was obtained from the patient/s for publication of this study and any accompanying images.

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of ectopic pregnancy. We selected patients diagnosed with CEP for further review. For patients with CEP, we analyzed patient characteristics, medical history, obstetric history, gestational age, symptomatology on presentation, levels of serum  $\beta$ HCG, risk factors, diagnostic, and treatment methods performed. Lastly, we analyzed estimated blood loss (EBL) for each patient, using the hemoglobin estimation loss formula.<sup>6</sup>

## RESULTS

During this period, a total of 260 patients were admitted with the diagnosis of ectopic pregnancy to our center. CEP was confirmed in 10 patients (Table 1).

The patient's age varied from 26 to 50 years, with a median of 36.5 years. The median gestational age at diagnosis was 7 weeks. Of the 10 patients with confirmed cervical ectopic pregnancy, nine of them have conceived spontaneously and one after an ART procedure. Eight patients had at least one potential risk factor for the CEP in their obstetric history. Four patients had symptoms of a CEP while six patients were asymptomatic and admitted only after ultrasonographic suspicion of CEP. The median value of serum  $\beta$ HCG, at the time of admission, was 81780.5 mIU/mL. Three patients were nulligravida. Patient characteristics, ultrasonographic findings, obstetrical history, levels of hemoglobin (Hgb) before and after the procedure, EBL, and length of hospital stay are presented in Table 2. Seven out of 10 patients with CEP lacked fetal cardiac activity (two of them underwent small-caliber hysteroscopy), and three patients had a viable cervical pregnancy (one of them underwent small-caliber hysteroscopy).

Three patients with CEP were treated with small-caliber hysteroscopy, while 7 patients underwent dilatation and curettage (D&C). Beriplast® fibrin glue was given as needed to provide additional hemostasis.

**Table 1.**

Cases of Ectopic Pregnancies with the Types of Ectopic Pregnancy and Their Percentage

Type of Ectopic Pregnancy	Number of cases (%)
Tubal	241 (92.7 %)
Cervical	10 (3.8 %)
Cornual	6 (2.3 %)
Caesarean Scar	3 (1.2 %)
Total = 260 (100%)	

## Hysteroscopic Management of CEP

Hysteroscopy was performed using a 3.8 mm hysteroscope (Richard Wolf, Knittlingen, Germany) with a 30-degree scope. Prior to hysteroscopy, we performed an ultrasonographic evaluation, where we identified the gestational sac (GS) inside the cervical canal (Figure 1A). All patients underwent laboratory analyses to evaluate baseline coagulation status. All patients had normal laboratory testing. All hysteroscopic procedures were performed under general anesthesia and all patients were consented for possible conversion to laparotomy. We utilized normal saline solution as the distention medium. In all cases, we identified the gestational sac and the implantation site inside the cervical lumen (Figure 1B).

### Case 1

A 26-year-old patient with a gestational age of 6 weeks and two days admitted to our center with the suspicion of CEP. She presented to us after a routine ultrasonographic examination performed at a local primary care center raised the suspicion of CEP. The only symptom she complained of was mild brown vaginal discharge. She had a history of a previous spontaneous abortion followed by D&C and an induced abortion at 22 weeks of pregnancy due to preterm premature rupture of membranes. The initial serum level of  $\beta$ HCG was 6392 mIU/mL. Pelvic examination did not reveal any significant abnormalities. The ultrasonographic examination revealed an empty uterine cavity with a GS in the cervical canal and an embryo with a Crown Rump Length (CRL) of 6.2 mm without cardiac motion. After examination of the vaginal vault with hysteroscopy, the 3.8 mm hysteroscope was introduced into the cervical canal and the GS was identified approximately 1.5 cm from the internal uterine os. An incision over the GS was performed using 5 French (Fr) operative hysteroscope with hysteroscopic scissors (Richard Wolf, Knittlingen, Germany). After the incision, products of conception were evacuated using the hysteroscopic forceps (5 Fr, Richard Wolf, Knittlingen, Germany). EBL was 0 mL. On postoperative day 1, the serum  $\beta$ HCG level dropped significantly to 2260 mIU/mL and the patient was discharged home.

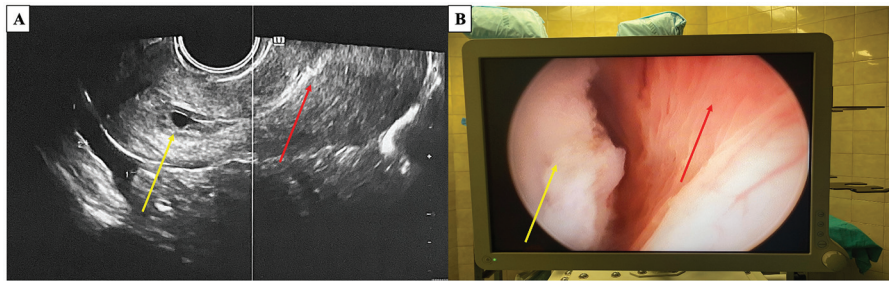
### Case 2

A 42-year-old patient at 7 weeks and 1 day of gestation was admitted to our hospital under the suspicion of CEP, which was observed during a routine first trimester ultrasonographic examination. The patient was asymptomatic. In her medical

**Table 2.** Patient's Characteristics, Symptoms, Ultrasonographic Features, and Treatment Methods

Case	Age	Obstetric History	Potential Risk Factor(s)	Weeks of Gestation	Serum $\beta$ HCG (mIU/mL)	Onset Symptoms	Ultrasonographic Features	Cardiac Activity	Treatment	Hospital days	Hgb before Procedure (g/dL)	Hgb after Procedure (g/dL)	EBL (mL)
1	41	P0G0	IVF/ET, 3laparoscopic cystectomies, tube ligation	7	12.701	Mild bleeding	7.4 mm GS in cervical canal with an embryo with CRL 4.4 mm	No	D&C	13	Nm*	Nm	Nm
2	26	P0G2	D&C	7	6.392	None	GS in cervical canal with an embryo with CRL 6.2 mm	No	Small-caliber hysteroscopy	2	135	135	0
3	26	P0G0	D&C	8	3.511	Bleeding without cramps	GS in cervical canal with an embryo with CRL 12 mm	No	D&C	6	122	121	30
4	35	P2G2	2 CS	8	103.089	None	GS in cervical canal with an embryo with CRL 12 mm	Yes	D&C	3	127	126	< 20
5	40	P2G3	2 CS, 1 D&C	6	4.798	None	GS in cervical canal without an embryo	No	D&C	7	Nm	Nm	Nm
6	50	P0G0	None	7	/	Cramping	GS in cervical canal with an embryo with CRL 7 mm	No	D&C	6	Nm	Nm	Nm
7	29	P2G3	D&C	9	/	Bleeding	GS in cervical canal with an embryo with CRL 17 mm	No	D&C	7	125	122	98
8	37	P0G1	D&C	6	13.737	None	GS inside the cervical canal with an embryo	Yes	D&C	4	142	140	70
9	42	P2G2	2 CS	7	9.768	None	10 mm GS in cervical canal with an embryo	Yes	Small-caliber hysteroscopy	2	140	139	< 20
10	27	P0G0	None	7	7.544	None	11 mm GS inside the cervical canal with an embryo	No	Small-caliber hysteroscopy	2	128	128	0

P, parity; G, gravidity; IVF/ET, in vitro fertilization/embryo transfer; D&C, dilatation and curettage; CS, cesarean section; GS, gestational sac; CRL, crown-rump length; Hgb, Hemoglobin; EBL, estimated blood loss/- the levels of serum  $\beta$ HCG were not available in the medical records; Nm, not measured.



**Figure 1. A.** Gestational sac with yolk sac and an echo of an embryo (Yellow Arrow) located in the cervix on ultrasonographic examination along with the empty uterine cavity (Red Arrow). **B.** Hysteroscopic view of the gestational sac (Yellow Arrow) in the lumen of the cervical canal (Red Arrow).

history, she had two previous cesarean section deliveries. The initial serum  $\beta$ HCG level was 9768 mIU/mL. The ultrasonographic examination revealed an empty uterine cavity with a GS inside the cervical canal and a CRL of 10 mm, with cardiac activity. Operative hysteroscopy (3.8mm) was performed as previously described in case 1 followed by evacuation of products of conception with hysteroscopic forceps. EBL was < 20 mL. The next morning levels of serum  $\beta$ HCG dropped to 1772 mIU/mL. The patient was discharged home after the procedure on postoperative day 1.

### Case 3

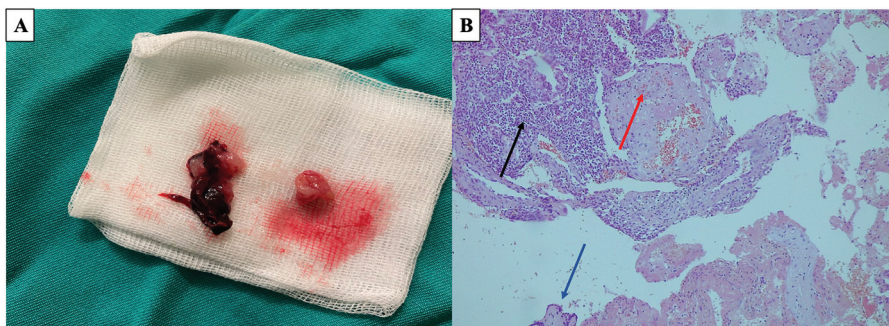
A 27-year-old patient at 7 weeks gestation presented to our center after a routine ultrasound revealed findings consistent for CEP. The patient was asymptomatic. The initial serum  $\beta$ HCG level was 7544 mIU/mL. The ultrasonographic examination showed an empty uterine cavity with a GS of 11 mm and fetal pole within the cervical canal, without cardiac activity. The gestational sac was identified with a small-caliber hysteroscope (3.8 mm). Operative hysteroscopy with the evacuation of products of conception was performed similarly to cases 1 and 2. EBL was 0 mL. On postoperative

day 1 serum  $\beta$ HCG level dropped to 1970 mIU/mL and the patient was discharged home.

The blood loss for all three cases was minimal and no additional hemostatic methods were required. All three patients were discharged 24 hours after the hysteroscopic procedure, with no apparent bleeding. After the procedure, all specimens (**Figure 2A**) were sent for histopathological examination. All of them showed decidual tissue and chorionic villi surrounded by endocervical epithelium (**Figure 2B**). The median number of hospital days for the patients treated with small-caliber hysteroscopy was 2, while the median number of hospital days for patients treated with D&C was 6.

## DISCUSSION

To our knowledge, this is the first published case series of successful CEP treatment solely by small-caliber hysteroscopy, without any additional procedures. Arguably, the main concern when managing CEP is the patient's wish to preserve fertility. Clinically, based on our retrospective review, parameters such as gestational age, values of serum  $\beta$ HCG, and the presence of fetal cardiac activity have to be taken into



**Figure 2. A.** Conception products after hysteroscopic evacuation. **B.** Histopathological examination of the obtained sample with decidual tissue (Red Arrow) and chorionic villus (Blue Arrow) surrounded by endocervical epithelium (Black Arrow), Hema-toxylin and Eosin x10.

consideration when choosing the best treatment route for the patient.<sup>2,7</sup> Our main conclusion based on our review of the literature and our center's experience is that an approach to each patient remains individual. Because CEP is a rare condition, there are no universally accepted protocols for the management of CEP.

Criteria for the ultrasonographic diagnosis of CEP were first described several decades ago.<sup>8</sup> No evidence of pregnancy inside the uterine cavity, hourglass shape of the uterus, endometrial decidual transformation, the presence of a gestational sac and/or placental tissue in the ballooned cervical canal, with or without fetal structures, and closed internal os is the quintessential sonographic finding in CEP. Additionally, the peritrophoblastic blood flow using color Doppler is an important criterion in the diagnosis of CEP, which is absent in cases of miscarriage.<sup>9</sup> Jurkovic et al. introduced the "sliding sign" to mark the difference between abortion and cervical pregnancy: under the gentle pressure with the vaginal probe, the products of conception will slide against the cervical canal in the cases of abortion.<sup>9</sup>

In all of the cases in our report, CEP was successfully diagnosed and confirmed with an ultrasonographic examination. Our experience underlines the importance of an expert sonographic examination in early pregnancy. A properly performed examination could prevent life-threatening complications and allow the conservative or minimally invasive treatment of these patients.

Although, reports suggest that CEP is the rarest form of ectopic pregnancy, with an overall incidence of less than 1%,<sup>1</sup> our study showed a CEP of 3.8% of all ectopic pregnancies. We do not think that this represents the real incidence of CEP. Our center is one of the largest regional tertiary-care units for obstetrics and gynecology and this finding may be attributed to a sampling error.

Hysteroscopy is now a well-established gold standard for evaluating and management of intrauterine pathology.<sup>10</sup> Additionally, hysteroscopy is regarded as one of the first steps in the diagnosis and treatment of infertility.<sup>10-12</sup> Furthermore, there are now numerous reports that highlight the cost-effectiveness of hysteroscopy.<sup>12,13</sup> Most importantly, the physician can easily "see and treat" pathology found at the time of hysteroscopic evaluation.<sup>10</sup>

The first described case of hysteroscopic resection of CEP, preceded by vasopressin injection, cervical suture, and ligation of uterine artery branch for the prevention of bleeding, was published by Ash and Farrel in 1996.<sup>14</sup> We have found a total of 16 published case reports or case

series regarding the hysteroscopic treatment of CEP. Roughly, these reports could be divided into three categories: management of CEP solely by operative hysteroscopy, hysteroscopic management after (un)successful methotrexate (MTX) therapy, and combination of hysteroscopy and ligation or uterine artery embolization.

It needs to be underlined that some authors decided to perform hysteroscopy after failed treatment with MTX. It has been suggested that one-third of the patients treated with MTX require additional invasive procedures.<sup>2</sup> On the other hand, it has been reported that treatment with MTX requires longer hospitalization, and is associated with potential side-effects.<sup>2,5</sup> Moreover, the time required for the normalization of serum  $\beta$ HCG levels could take up to several weeks.<sup>7</sup> Based on the published case series, gestational age > 9 weeks, the presence of fetal heart activity, serum levels of  $\beta$ HCG > 10,000 mIU/mL, and CRL > 10 mm are all associated with poor response to MTX therapy.<sup>7,15</sup> Our patients who underwent small-caliber hysteroscopy had gestations of approximately 7 weeks, were asymptomatic at presentation and had initial  $\beta$ HCG levels < 10,000 mIU/mL.

Patients who underwent small-caliber hysteroscopy in our case series did not receive MTX and were discharged the day after the procedure. Even though some authors report successful MTX treatment before hysteroscopic resection of CEP,<sup>16,17</sup> the length of hospital stay from these reports exceeds the number of days presented in our series. The findings of a shorter hospital stay along with minimal blood loss encountered during our procedure strengthens the cost-effectiveness and safety of small-caliber hysteroscopy in the treatment of CEP.

Furthermore, to our knowledge, only Tanos et al. described the use of a hysteroscope of a smaller caliber (2.8 mm) than the 3.8 mm hysteroscope used in our series.<sup>18</sup> Combining both series, seven CEPs were successfully treated with a small-caliber hysteroscope, without bleeding complications or need for a second operation. Moreover, mild to moderate bleeding after the procedure in the series by Tanos et al. was controlled by local application of Surgicel<sup>®</sup>.<sup>18</sup> The use of hemostatic agents in gynecological interventions has many advantages, and recently, management of bleeding in the treatment of CEP with hemostatic agents similar to tissue glue has been reported.<sup>19</sup> We recommend future studies regarding combined treatment with small-caliber hysteroscopy and hemostatic agents since this could have a beneficial effect in terms of safety in an already minimally invasive procedure.

On the other hand, gynecologists should be prepared for sudden, massive, and life-threatening bleeding, as

a potential complication of CEP. Uterine artery embolization (UAE) has been described as a safe and efficient procedure for the prevention of massive hemorrhage in patients with uterine fibroids, gestational trophoblastic diseases, and bleeding of obstetrical causes.<sup>20,21</sup> Recently, some authors published reports of successful treatment with the combination of laparoscopic uterine artery ligation and clipping, followed by hysteroscopic resection of CEP.<sup>22</sup> While, both UAE and ligation of the uterine artery have many advantages, there is still insufficient data regarding its impact on future fertility with reports of amenorrhoea, pain, uterine necrosis, and pelvic infection among the potential consequences of these methods.<sup>23</sup>

Small-caliber hysteroscopic treatment also has to be approached with caution and should be performed only by an experienced and skilled surgeon. The procedure should be performed in an operating room under general anesthesia. Moreover, hemostatic agents, such as Beriplast® tissue glue and the ability to perform laparotomy should be available if unexpected bleeding occurs.

The main limitation of our study is the small number of subjects. Even though we successfully treated three patients with the small-caliber hysteroscopy, we believe that future multicenter-based studies with a larger number of subjects with CEP treated solely with this procedure are needed.

## CONCLUSIONS

It is our experience that small-caliber hysteroscopy is a feasible and low-risk technique in the hands of an experienced hysteroscopist to manage CEP, especially in stable, asymptomatic patients, less than 10 weeks gestational age, who are desiring future fertility. This technique offers benefits such as shorter hospital stay, minimal blood loss, and short recovery time. Future multicenter randomized controlled trials are necessary to further evaluate its safety and efficacy compared to other techniques.

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