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Uterine Artery Embolization Combined with Dilation and Curettage for the Treatment of Cesarean Scar Pregnancy: Efficacy and Future Fertility

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Abstract
Purpose To investigate the efficacy and safety of uterine artery embolization (UAE) followed by dilation and curettage (D&C) as a treatment for cesarean scar pregnancy (CSP) and to assess pregnancy outcomes after the treatment.
Materials and Methods We retrospectively analyzed 33 CSP patients treated with UAE followed by D&C. The serum level of beta human chorionic gonadotropin (β-hCG) normalization, hospitalization, menstruation, and successful pregnancy after treatment was assessed as clinical and pregnancy outcomes.
Results A total of 33 patients were initially treated without severe complications. However, four patients required additional systemic chemotherapy. β-hCG normalization took 35.5 ± 14.9 days (range 13–79), and the hospitalization was 6.5 ± 2.5 days (2–15). All patients resumed normal menstruation after 36 ± 19.2 days (12–86). Of 16 of 33 patients who desired pregnancy after the treatment, seven patients (43.8%) had uneventful parturition.
Conclusions UAE combined with D&C was efficient and safe for CSP management. This minimally invasive procedure may be considered as one of the treatment options which enable preservation of fertility after treatment.

Keywords Cesarean scar pregnancy · Dilation and curettage · Fertility · Pregnancy outcomes · Uterine artery embolization

Synopsis Uterine Artery Embolization combined with Dilation and Curettage is preferred as a safe and efficient treatment in 33 cases with cesarean scar pregnancy.

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Introduction

Cesarean scar pregnancy (CSP) is a rare form of gestation, which carries a high risk of uncontrollable bleeding and hysterectomy. In 1978, Larsen and Solomon first found that the gestational sac (GS) sometimes implanted in a previous cesarean scar [1]. The prevalence of CSP was estimated to be 1 in 1800–2216 pregnancies, and 6.1% of all ectopic pregnancies had a history of at least one cesarean section (CS) [2]. The incidence of CSP has been increasing

recently. The reasons for this trend are uncertain, but possible explanations may be the increased frequency of cesarean delivery and increased detection due to advances in ultrasound (US) and magnetic resonance imaging [3, 4].

Recent studies have reported that some of the expectant CSPs lead to severe maternal morbidity, i.e., massive hemorrhage, shock, uterine rupture, and eventually result in hysterectomy with a loss of fertility [5, 6]. Because of this, termination of the CSP in the first trimester has been highly recommended. Several management approaches to preserve fertility and prevent severe consequences have been recently reported, including surgical and non-surgical intervention. However, optimal management guidelines of CSP have not been established.

Uterine dilation and curettage (D&C), which is a surgical intervention for CSP, has not been recommended as a primary treatment due to high risk of hemorrhage, which may result in emergency laparotomy and possible hysterectomy [7]. However, recent studies noted that combining uterine D&C with UAE may be a safe approach and that combination therapy may have advantages of preserving future fertility and reducing maternal mortality with a high success rate [8, 9].

The purposes of this study were to estimate the clinical efficacy and safety of UAE followed by D&C treatment for CSP and to investigate the pregnancy outcomes of the women who underwent this treatment. We also conducted a literature review for the outcomes for treatments of CSP.

Materials and Methods

Clinical Study

We performed this retrospective analysis using clinical records of 33 patients diagnosed with CSP from September 2006 to October 2017 in our institution. This study was approved by our institutional ethical committee.

Diagnosis of CSP was based on the history of a prior CS, an elevated serum level of β-hCG, and transvaginal ultrasound examination. The US image of all 33 cases met the following criteria: (1) absence of intrauterine gestation and empty cervical canal with clearly visible endometrium; (2) a GS located in the anterior isthmus, surrounded by cesarean scar tissue and with or without a thin myometrial layer between the bladder and the GS; (3) a GS with or without fetal pole with or without cardiac activity; (4) on Doppler US, a GS embedded in a scar defect surrounded by vascular flow characterized by high velocity and low impedance [10] (Fig. 1).

The 33 patients underwent UAE followed by D&C within 24 h. After local anesthesia, catheterization was carried out via the right femoral artery with a 5F-sheath

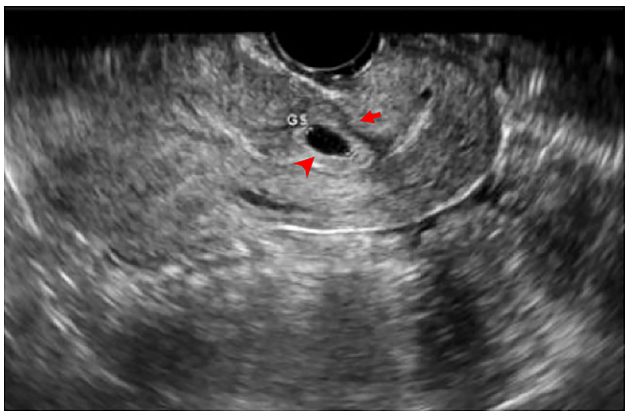

Fig. 1 A 38-year-old woman: A cesarean scar pregnancy (CSP) demonstrated by transvaginal ultrasound (US) (sagittal longitudinal section) showing an empty uterine cavity and cervical canal, and the gestational sac (GS) implanted in the lower segment dehiscence of the anterior myometrium (arrow head). The diameter of GS was 11 mm (5 weeks + 1 day pregnancy). Arrow is the scar of a previous cesarean section (CS). Serum β-hCG level before the treatment was 12066 IU/L

introducer (Medikit Super Sheath, Tokyo, Japan). First, we performed initial aortography at the level of renal arteries with a 4F-pigtail catheter (Terumo Clinical Supply Co. Ltd., Gifu, Japan) to identify the uterine arteries. A 5F-cobra catheter (Medikit Co. Ltd., Tokyo, Japan) was introduced over a .035-inch guidewire (Terumo Clinical Supply Co, Ltd., Gifu, Japan) to assess the internal iliac arteries and branches to uterine arteries. Bilateral uterine arteries were selected with the 5F-cobra catheter or a micro-catheter (Estream 2.0; Toray Medical Co. Ltd., Tokyo, Japan), and super-selective embolizations were performed with gelatin sponge particles (Serescue; Nippon Kayaku Co. Ltd., Tokyo, Japan), which were absorbable and nonpermanent embolic materials. Immediately after, post-embolization angiography was conducted to confirm complete vessel occlusion (Fig. 2). Within 24 h after UAE, experienced gynecologists performed D&C under ultrasound guidance and paracervical local anesthesia for all patients. GS and clot were removed via forceps and was curetted gently to decrease the risk of uterine scar rupture and the residual villous. The patients who have a serum level of β-hCG more than 3000 mIU/L at 10th day or more than 1000 mIU/L at 28th days after D&C required as an additional treatment (oral MTX at 50 mg/day for 5 days).

The serum level of β-hCG, blood loss, side effects of the treatment, menstruation, and hospitalization length of all patients was recorded during the follow-ups. Serum level of β-hCG (normal range less than 5 mIU/mL) was assessed before the intervention, on the day after treatment, every 3 days until discharge, and weekly until normalization to < 5 mIU/mL. At the same time, US examination was performed routinely to detect residual until the mass had

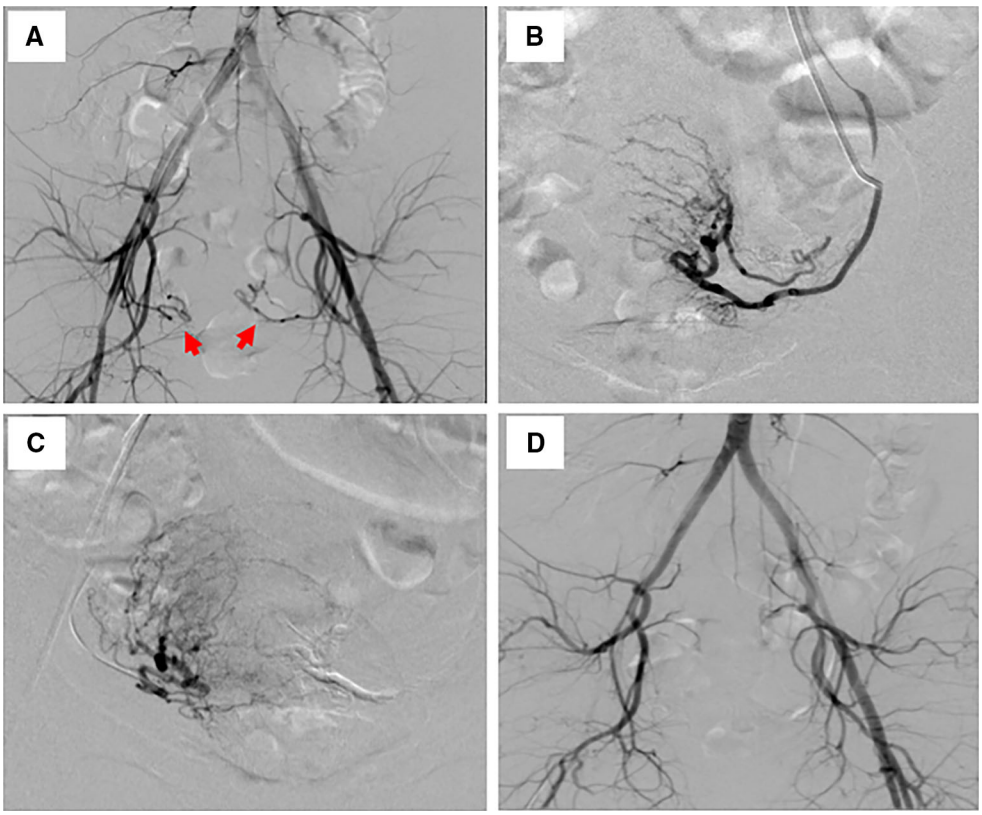

Fig. 2 Digital subtraction angiogram of a patient with cesarean scar pregnancy (CSP) who received transcatheter uterine embolization. **A** Before embolization; angiogram shows the uterine blood supply (arrows). **B**, **C** Before embolization: angiograms of uterine arteries on both sides. **D** After embolization, the uterine blood supply disappeared. After embolization, dilation and curettage (D&C) was performed

been completely disappeared. All patients were followed up in the outpatient clinic of our institution after discharged the hospital. The last follow-up evaluation was 3 months after the D&C. After that, we confirmed whether the patient was pregnant by letter or telephone to the patient or the announcement from the family doctor.

In this study, normalization of serum β-hCG levels, no severe complications (hysterectomy and/or hemorrhage $\geq$ 1000 mL), and preservation of fertility were considered as successful outcomes. The pregnancy outcomes were assessed for the patients who desired to conceive. These patients were divided into two groups: group (I) conceived again and group (II) unable to become pregnant to compare potential factors for successful pregnancy.

The clinical characteristics from the records, including patient age, gravidity, the number of previous CS, time interval since last CS, gestational age (GA), size of GS, blood loss, serum level of β-hCG, and clinical findings, were reviewed. Student *t* test and Mann–Whitney *U* test were employed based on results of Kolmogorov–Smirnov and Levene tests to compare potential factors for the successful pregnancy. We used SPSS 24 software (SPSS, Inc., IL), and $p < .05$ was defined as being statistically significant.

We performed a literature review on available CSP reports until November 2016 using key terms of "cesarean scar pregnancy," "reproductive," and "pregnancy outcomes" from PubMed and Google Scholar. The inclusion criteria for the reports were: (1) research using the most common approaches such as methotrexate (MTX), D&C, hysteroscopy/laparoscopy management, and UAE for the CSP; (2) publications in the English language; (3) studies including more than 20 patients. We did not include case reports.

Results

Clinical Study

The clinical features of 33 patients (33 ± 4.2 years old; range 25–39) treated with UAE followed by D&C are shown in Table 1. In particular, 18 of 33 (54.5%) patients had a single previous CS, 13 (39.4%) had two, and two

Table 1 Clinical features of patients treated with UAE followed by D&C (n = 33)

Characteristic	Mean ± SD
Mean age (years)	33 ± 4.2 (range 25–39)
Gravidity (number)	1.8 ± .8
Previous CS (number)	1.5 ± .6
1	18 (54.5%)
2	13 (39.4%)
3	2 (6.1%)
Time interval since last CS (years)	4 ± 2.5 (range .7–9)
≤ 2	10 (30.3%)
2 to 5	13 (39.4%)
≥ 5	10 (30.3%)
GA (day)	43.9 ± 8.3 (range 33–72)
< 40	9 (27.3%)
40–70	23 (69.7%)
> 70	1 (3.0%)
Serum level of β-hCG before treatment	26,838.8 ± 22,254.8 (range 369.9–77,702)
< 10,000	7 (21.2%)
10,000–30,000	15 (45.8%)
> 30,000	11 (33.3%)
GS size (mm)	18.5 ± 9.4 (range 8–49.6)
Fetal cardiac activity (positive)	15 (45.5%)
Myometrium thickness (mm)	10.1 ± 4.5 (range 3.3–22.1)

Unless otherwise indicated, data are expressed as mean ± SD (range), number (percentage); β-hCG, β-human chorionic gonadotropin; CS, cesarean section; *CSP* cesarean scar pregnancy, *GA* gestational age, *GS* gestational sac, myometrium thickness, at the implantation site between sac of the CSP and wall of the bladder

(6.1%) had three. The estimated GA at the time of presentation was 43.9 ± 8.3 days (range 33–72).

The clinical outcomes after CSP treatments are presented in Table 2. The mean time for the serum β-hCG level normalization (< 5 mIU/mL) was 35.5 ± 14.9 days (13–79). The mean blood loss was 28.2 ± 17.1 (range 3–65) mL. The average time of hospital stay was 6.5 ± 2.5 (range 2–15) days.

Four (12.1%) patients required additional treatment (oral MTX at 50 mg/day for 5 days) due to insufficient decrease in serum β-hCG level on the 10th day after treatment. The normalization time for patients who required additional treatment was 58.3 ± 21.3 days (34–79). Only two patients had a fever and slight pelvic pain, which quickly disappeared after symptomatic therapy. There was no case with severe complications during treatment and follow-up.

In all patients, the uterus was preserved. Seven pregnancies (43.8%) from the 16 patients who planned their next pregnancies delivered successfully by CS (Table 3). Significant differences were found for the serum level of β-

Table 2 Clinical outcomes after treatment of CSP

Characteristic	Mean ± SD
Serum level of β-hCG normalization (days)	35.5 ± 14.9 (range 13–79)
Hospitalization (days)	6.5 ± 2.5 (range 2–15)
Total blood loss (ml)	28.2 ± 17.1 (range 3–65)
Additional treatment (oral MTX)	4/33 (12.1%)
Time for menstruation to resume	36 ± 19.2 (range 12–86)

Unless otherwise indicated, data are expressed as mean ± SD (range), number (percentage); β-hCG, β-human chorionic gonadotropin

CSP cesarean scar pregnancy, *MTX* methotrexate

Table 3 Pregnancy outcomes in women with previous CSP

Characteristic	Results
Pregnancy rate	7/16 (43.8%)
Time between CSP treatment and pregnancy (months)	8.4 ± 3.6 (range 4–13)
Secondary infertility rate	9/16 (56.3%)
Live birth rate	7/7 (100%)
Miscarriage rate	0/7 (0%)
CS rate	7/7 (100%)
Placenta accrete rate	0/7 (0%)

Unless otherwise indicated, data are expressed as number (percentage) or (range). *CS* cesarean section, *CSP*, cesarean scar pregnancy

Secondary infertility; after treatment women with CSP could not get pregnant. However, desired to pregnancy during follow-up

hCG normalization time ($p < .02$) and GS size ($p < .01$) between two groups (Table 4).

Literature Review

We found five published data which met the inclusion criteria of the present study and tried to address pertinent concerns on the clinical and subsequent pregnancy outcomes of women with a previous CSP. We assessed the clinical outcomes of 303 patients from six studies including the present study (Table 5). Among the articles reviewed, 30% of patients had undergone multiple previous CS, whereas 70% of patients had undergone one previous CS. The success rate (defined as the efficacy of first-line treatment) ranged from 27 to 100%, and there was a wide variation in the complication rate (0–90.1%). The complication rate was the highest (90.1%), when patients were initially treated by D&C [11]. However, in the study by Ben Nagi et al. the complication rate was only 4% after D&C [12]. Even when local MTX treatments were performed along with D&C, the complication rate was still high (16%) [13]. Regarding laparoscopic management, length of hospitalization was 2–3.5 days and normalization of serum β-hCG levels was 17 days without any complications (Table 5) [14, 15]. Although hysteroscopic managements showed similarly short time of hospitalization and normalization of serum β-hCG levels at 3.8 and 27 days, hysteroscopic management had a complication rate of 5.1 and 25.6% of patients required additional treatment [14].

Subsequent pregnancy outcomes were analyzed for the 73 patients who desired to conceive after treatment (Table 6). The subsequent conception rate (number of women who got pregnant/number of women who desired to conceive) ranged from 5 to 88%, and the average rate of subsequent conception was 41% with 8.3 months after the CSP treatment. The live birth rate among the studies ranged from 43 to 100% with an average of 86%.

Table 4 Analysis of potential factors in favor of successful pregnancy

Characteristic	Group I ($n = 7$)	Group II ($n = 9$)	p value
Blood loss (mL)	30.4 ± 12.2	37.9 ± 16.7	.34
Age (years old)	29.6 ± 3.1	33.2 ± 3.6	.05
Previous CS (number)	1.7 ± .7	1.3 ± .5	.25
GS size (mm)	11.6 ± 3.5	20.6 ± 11.7	*.01
Time interval since the last CS (years)	2.4 ± 1.1	3.6 ± 2.4	.23
GA (days)	41.7 ± 8.8	46.1 ± 9.9	.56
Serum level of β-hCG normalization (days)	27 ± 11.31	46.9 ± 18.5	*.02
Time for menstruation to resume (days)	31.3 ± 14.2	39.4 ± 20.5	.40
Fetal cardiac activity (positive)	42.8% (3/7)	55.6% (5/9)	.64
Additional treatment (MTX oral administration)	0/7 (0)	3/9 (33.3%)	.10

Unless otherwise indicated, data were expressed as mean ± SD, number (percentage); β-hCG, β-human chorionic gonadotropin

CS cesarean section, *GS* gestational sac, *GA* gestational age

*statistically significant

Table 5 β-hCG level, treatment, and outcomes in conservatively treated CSP

References	Cases (*n*)	Average serum level of β-hCG (mIU/ml)	Initial treatment no. of cases	Additional treatment *n* (%)	Success rate (%)	Normalization time of β-hCG (days)	Hospitalization (days)	Complication rate (%)
Yang et al. [11]	66	440–129,520	D&C (*n* = 11)	Hysterectomy 3 (27)	27	27.3	22	90
				Laparotomy 1 (9)				
			Systemic MTX (*n* = 17)	Hysterectomy 2 (12)	58.8	44.3	16.7	42
				MTX or D&C 5 (29)				
			UAE + Local MTX (*n* = 38)	Re-embolization 2 (5) D&C 24 (63)	89.5	28.1	12.5	11
Wang et al. [13]	71	13,576	Local MTX (*n* = 21)	Laparotomy 11 (52)	76.2	38.5	N/A	43
		8323.5	Local MTX + D&C (*n* = 50)	Laparotomy 5 (10)	90	25	N/A	16
Wang et al. [14]	71	36,759	Laparoscopy *n* = 32	0 (0)	100	17	3.5	0
		28,127	Hysteroscopy N = 39	Laparoscopy 4 (10)	74.3	27	3.8	5.1
				UAE + MTX 3 (8)				
				Hysteroscopy 3 (8)				
Wang et al. [15]	22	30,288	Laparoscopy = 22	0 (0)	100	N/A	2	0
Ben Nagi et al. [12]	40	N/A	D&C (*n* = 28)	Hysterectomy 1 (3.5)	N/A	N/A	N/A	4
			Local MTX (*n* = 9)	D&C 3 (33)	67		N/A	N/A
			Expectant (*n* = 3)	Hysterectomy 2 (67)	0		N/A	67
Present study	33	26,839	UAE followed D&C (*n* = 33)	MTX oral 4 (12)	100	35.5	6.5	0
Average		29,842			78.3	30.3	9.6	
Total	303		303	73/303 (24)				

The success rate (as a percentage) was defined as the efficacy of first-line treatment; complications rate (as a percentage) hysterectomy and/or hemorrhage ≥1000 mL

D&C dilation and curettage, *CS* cesarean section, *CSP* cesarean scar pregnancy, *MTX* methotrexate, *UAE* uterine artery embolization

Discussions

The management of CSP can be surgical or pharmacological, the latter mainly consisting of systemic or local administration of MTX [2]. Surgical management includes D&C, UAE, hysteroscopy, and laparoscopic management to excise GS from the uterine scar [16]. In our analysis of comparison, one of six studies showed fast recovery, short follow-up, and a rapid normalization of β-hCG by hysteroscopy/laparoscopy management [14]. However, these procedures required a skilled surgeon and hemodynamically stable patients [10, 17, 18]. Seow KM et al. suggested that laparotomy may be the best option for CSP when the circumstances are not ideal [19]. However, laparotomy may have drawbacks of a larger surgical wound, longer

Table 6 Subsequent pregnancy outcomes among pregnant women with previous CSP

References	Cases (*n*)	Subsequent Conception *n* (%)	Live birth rate, *n* (%)	Deliveries *n*	Recurrent CSP *n* (%)	Complications (*n*)	Time between CSP treatment and subsequent pregnancy (months)
Yang et al. [11]	66	2/14 (14)	2/2 (100)	2/2 CD	0/14 (0)	0	N/A
Wang et al. [13]	71	N/A	N/A	N/A	N/A	N/A	N/A
Wang et al. [14]	71	N/A	N/A	N/A	N/A	N/A	N/A
Wang et al. [15]	22	1/19 (5)	1/1 (100)	1/1 CD	0/1 (0)	0	6.5
Ben Nagi et al. [12]	40	21/24 (88)	9/21 (43)	9/9 CD	1/21 (5)	7 abortion	5.3
Present study	33	7/16 (44)	7/7 (100)	7/7 CD	0/7 (0)	0	8.4
Average							8.3
Total	303	31/73 (41)	26/31 (86)	19/19	1/22 (4.5)	7	

Subsequent conception rate (number of women who got pregnant/number of women who desired to conceive)

CD cesarean delivery, *CSP* cesarean scar pregnancy, *N/A* not available

period of hospitalization, and longer recovery time than other options [20].

UAE combined with MTX is one of the alternative treatments for the patients with CSP [11]. However, it takes a long time for the GS to be spontaneously reabsorbed. Additionally, there is still a risk of massive hemorrhage with the gradual reestablishment of collateral circulation. Thus, D&C can be required as an additional treatment after UAE. MTX treatment is the most popular treatments of CSP because of the prompt response and favorable side effects profile. However, studies evaluating the outcome of MTX modality have reached conflicting results such as a slower decline in serum β-hCG levels, potential massive bleeding, and required additional treatment [11, 13].

In our study, four (12.1%) patients showed inadequate decline of B-hCG and were treated with additional treatment. The decline of B-hCG is related to the degree of invasion of trophoblastic cells into the CS scar and myometrium, which could not be removed by D&C alone [21]. Thus, the normalization time for serum β-hCG level in those patients was longer than the patients who did not require further treatment.

Pregnancy outcome after the treatment of CSP is a critical concern for patients who are keen to preserve their fertility. Also, there has been no consensus provided on the optimal timing for a pregnancy after CSP treatment. In our study, seven (44%) patients conceived 8.4 ± 3.6 months (4–13) after the treatment without any complications. Also, the live birth rates were 100%, which was higher than those found in the previous studies [11, 15]. Ben Nagi et al. reported that a total 21 of 24 (88%) had subsequent conceptions. However, uneventful parturition was limited to nine (43%) (Table 6) [12].

Fertility is affected by a variety of factors including but not limited to the woman's age and ovarian reserve [22]. Du et al. suggested that larger sac size may increase the risk of complications requiring additional treatment. Additional treatment may lead to undesired outcomes such as complications or damage to future fertility [23]. Timor-Tritsch et al. reported that earlier treatment for CSP led to a better outcome [24]. In our study, three of nine patients (33.3%) from group II required additional MTX treatment, while no patient from group I required additional treatment. Statistically significant differences in GS size were also found between the two groups. Steirteghem et al. found that the decline in fertility became clinically relevant when women reached their mid-thirties [25]. In our study, the mean age of patients in the two groups had borderline significance.

Several researchers suggested that UAE treatment might be associated with decreased ovarian reserve and adverse effects on fertility and did not recommend UAE for patients of reproductive age [10, 26, 27]. However, Wei Lin et al. and other researchers found that pelvic arterial embolization did not adversely affect fertility [28–30]. Our findings showed a pregnancy rate of 44% with prompt normalization of β-hCG levels and preservation of fertility without severe complications.

Our study had some limitations. First, the number of the cases was small because of the low incidence of CSP during the study period. Second, the study was retrospective in nature and information on reproductive outcome

was incomplete, since parturition was in different hospitals. Further research with more patients and longer follow-up periods (randomized cohort study) are needed to acquire objective conclusions for advanced findings.

Our results are similar to Zhang et al. [31] who indicated that UAE followed by D&C may be a safe and efficient treatment for CSP. Also, this approach potentially enables preservation of fertility and subsequent parturition.

Gonzalez et al. suggested that shorter intervals between the cesarean pregnancy and subsequent pregnancy may increase the risk of having CSP and placenta accrete [10]. However, we feel that impact of the interval time remains unclear. In our study, the range between the previous CS and CSP was 4 ± 2.5 (range .7–9) years, which was similar to previous studies [2, 12, 15, 32]. Jurkovic et al. demonstrated that CSP cases were more likely to happen after multiple CS [33]. However, our results did not support the hypothesis that multiple CS is a risk factor for CSP.

Conclusions

UAE combined with D&C was efficient and safe for CSP management. This minimally invasive procedure may be considered as one of the treatment options which enable preservation of fertility.

Authors' Contributions All authors participated in the study design. AT collected the data, carried out the analysis, and drafted the manuscript. HT supervised the overall study process. HT and YT revised the manuscript. AT-T checked English correction of the manuscript. All authors contributed to the writing of the final manuscript and approved it to be published.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest and nothing to disclose.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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