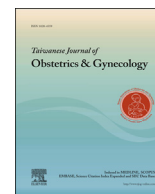




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## Original Article

## Uterine artery embolization with and without local methotrexate infusion for the treatment of cesarean scar pregnancy



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## ABSTRACT

**Objective:** To compare the clinical value of uterine artery embolization (UAE) with local methotrexate (MTX) infusion to embolization without MTX in the treatment of cesarean scar pregnancies (CSPs).

**Materials and methods:** From January 2009 to December 2013, 50 patients with CSP treated with UAE receiving or not receiving local MTX infusion prior to curettage were analyzed retrospectively. Twenty-two patients were offered UAE with local MTX infusion prior to curettage (UAE + MTX group), whereas 28 patients received UAE alone prior to curettage (UAE group). Clinical data and the outcomes were analyzed, followed by a brief review of the published literature summarizing what is known about UAE with and without MTX for the treatment of CSP.

**Results:** UAE was successful in 42 of 50 cases (84%), with complications occurring in only five patients. There were no significant differences in the success rate, complication rate, recovery time, or hospitalization costs between the UAE + MTX group and the UAE group. However, blood loss in the UAE + MTX group was significantly higher than in the UAE group.

**Conclusion:** UAE with or without local MTX infusion might be an effective treatment for CSP. Compared with UAE alone, UAE with local MTX infusion did not dramatically improve the therapeutic effect of UAE. A larger and more comprehensive random control study is warranted to better evaluate the therapeutic effects of UAE in the treatment of CSP.

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## Introduction

Cesarean scar pregnancy (CSP) is a rare but potentially life-threatening complication of a previous cesarean birth, in which the gestational sac is implanted at the site of the previous cesarean scar and is surrounded by uterine muscular fiber, scar tissue, and the thin myometrium adjacent to the bladder [1,2]. CSP may lead to excessive hemorrhaging, shock, and/or uterine rupture with the potential necessity for hysterectomy; in the worst case, CSP can result in maternal death [3,4]. Therefore, it is imperative that CSP be diagnosed and effectively treated as early as possible. The number of identified CS pregnancies ranges from 1/1800 to 1/2216 of every pregnancy [5,6], and is likely to exponentially rise in the near future, because of the increasing rate of cesarean delivery

worldwide and enhanced detection through the widespread use of transvaginal ultrasound [7,8].

However, to date, the optimal management of CSP remains to be determined. In this study, the clinical value of uterine artery embolization (UAE) with or without local methotrexate (MTX) infusion prior to curettage in the treatment of CSP are discussed, along with a brief review of the published literature on the management of CSP.

## Materials and methods

## Patients

This study, which was approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province, Zhejiang, China is a retrospective case series of 50 patients diagnosed with CSP treated over a period of 5 years (from January 2009 to December 2013). Patients with a ruptured uterus, inevitable abortion, active inflammation, severe cardiac, lung, kidney, or liver disease, or allergy to iodinated contrast medium, MTX, or embolic material were excluded. All

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patients were given extensive counseling, and written informed consent was obtained from participants prior to the treatment. The medical records and ultrasound images of all patients with CSP were collected from the original hospital charts, operation notes, and outpatient medical records via telephone questionnaires.

The average patient age was  $31.68 \pm 4.58$  years (range 22–40 years). The average time between CSP and previous cesarean delivery was  $4.87 \pm 3.04$  years (range 0.6–12 years). In terms of the number of cesarean deliveries prior to CSP, 38 patients had one, 11 patients had two, and one patient had three. The range of symptoms was wide. Twenty-six patients complained of intermittent slight vaginal bleeding, in which five cases were transferred to our hospital because of a failed artificial abortion, and nine cases suffered from excessive vaginal hemorrhage owing to misdiagnosis and underwent dilatation and curettage (D&C) or medical abortion prior to referral from another hospital. Three patients only experienced light abdominal discomfort, and 12 were asymptomatic.

### Diagnosis

Alongside a positive pregnancy test, CSP was confirmed by the following transvaginal ultrasound criteria [9–11]: (1) an empty uterine cavity without contact with the sac, (2) a clearly visible empty cervical canal without contact with the sac, (3) the presence of the gestational sac in the anterior uterine isthmus with or without a fetal pole or fetal cardiac activity (depending on the gestational age), and (4) an absent or diminished myometrial layer between the bladder and the sac (Figure 1).

### Procedure

UAE with or without local MTX infusion before curettage was performed. A right transfemoral approach was used for artery access, and the uterine artery was selectively catheterized with a 5F Yashiro catheter (TERUMO, Tokyo, Japan) and embolized with gelfoam sponge particles (1–2 mm in diameter), with or without 25 mg of MTX infused bilaterally into via each uterine artery for a total of 50 mg prior to the embolization procedure. Uterine artery angiogram was performed prior to and after UAE. Embolization was performed until the bilateral uterine arteries were occluded (Figure 2). Curettage was performed under the guidance of abdominal ultrasound 24–120 hours later by qualified doctors.

### Treatment assessment and follow-up

The dynamic levels of serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) were determined every 3 days until the level had decreased by > 50% from pretherapy levels, then weekly until levels

returned to normal. Ultrasound was used to monitor the size of the gestational mass weekly until serum  $\beta$ -hCG had returned to normal levels, then monthly until the mass had disappeared. The outcomes of subsequent patient reproduction were recorded. Failure of the initial treatment was considered in the case of complications, such as significant vaginal bleeding (blood loss > 200 mL), when 7<sup>th</sup> day serum  $\beta$ -hCG continued to rise or decreased by  $\leq 50\%$ , or when the gestational mass became larger than pretherapy levels. In these cases, additional therapies were given. All patients were asked not to have intercourse until termination of the CSP was confirmed.

### Data analysis

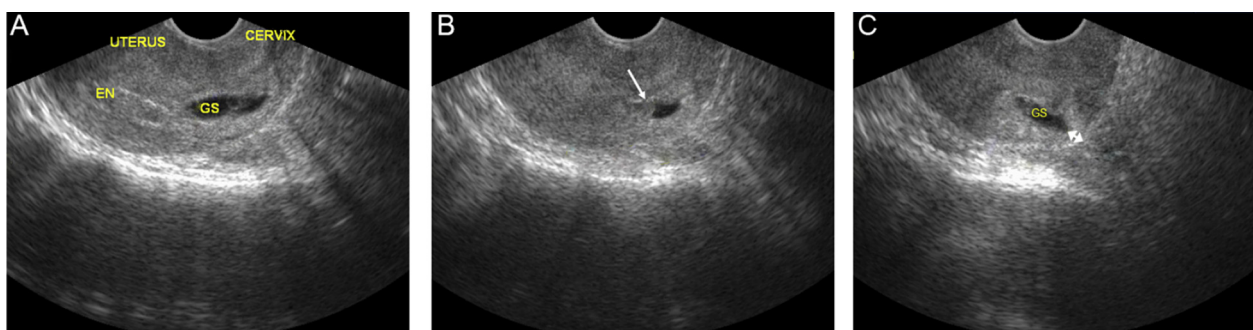
Mean  $\pm$  standard deviation ( $\bar{x} \pm S$ ) is presented for continuous and ordinal data, and categorical data are presented as the absolute count and percentage. The Chi-square test was used to compare categorical data. The two-sample *t* test was used to compare continuous and ordinal data. SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. A *p* value < 0.05 was considered statistically significant.

### Results

Fifty patients underwent UAE with or without local MTX infusion prior to curettage. This was successful in 42 cases (84%); eight cases required additional treatments with complications occurring in five cases; four of them were complicated with severe vaginal bleeding during curettage and were given hysterotomy. Post-operative pathologic examination of excised CSP specimens from these four patients showed clusters of trophoblast cells invading the myometrium. One patient's gelatin sponge separated from the uterine artery and embolized the right leg after UAE. Therefore, this patient went to other hospitals in Shanghai, China for a second UAE upon request. In the remaining three cases, treatments were considered a failure: In the first case, the patient was given an additional intra-amniotic MTX injection (50 mg) and later a second D&C. In the second case, the patient underwent systemic MTX treatment (50 mg/m<sup>2</sup>) and later another D&C. In the third case, the patient underwent hysterotomy after extensive counseling.

Among the 50 patients, 22 patients were offered UAE combined with local MTX infusion prior to curettage (UAE + MTX group), and 28 patients received UAE only prior to curettage (UAE group). The clinical characteristics and findings of the two groups are presented in Table 1.

There was no significant difference in the serum  $\beta$ -HCG levels, gestational age, diameter of the sac, or myometrium thickness between the two groups. In the UAE + MTX group, 77.3% cases were successfully treated, representing a lower success rate than in the



**Figure 1.** Transvaginal ultrasound image of a cesarean scar pregnancy at 7 postmenstrual weeks. (A) Empty uterine cavity with gestational sac between cavity and cervix. (B) Triangular shape of the sac; the embryonic pole and fetal cardiac activity are visible (arrow). (C) Gestational sac embedded in the scar; thin (3 mm) myometrium (arrow) between the sac and bladder.

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