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Management of Cesarean Scar Pregnancy: A Case Series

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Objective To survey effective treatment strategies for cesarean scar pregnancy (CSP).

Methods The clinical data of 78 patients diagnosed with CSP from January 2010 to December 2013 were reviewed.

Results Among these patients, 17 patients were first treated at our hospital; of them, 2 were misdiagnosed. The other 61 patients were referred from other hospitals; of them, 21 were initially misdiagnosed. There were 9 patients who were treated with laparotomy, 50 patients with curettage after uterine artery embolization (UAE) with or without local methotrexate (MTX) infusion, 10 patients with dilatation and curettage, 6 patients with transvaginal sonographic guided local intragestational MTX injection, and 3 patients with systemic MTX injection. All patients finally recovered. Patients with excessive vaginal hemorrhage underwent either emergency UAE treatment or laparotomy. These two treatments had similar success rates (81.82% vs. 100%, $\chi^2=0.289$, $P>0.05$).

Conclusions The accurate diagnosis of CSP is important. Curettage after UAE with or without local MTX infusion is a safe and effective method.

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CESAREAN scar pregnancy (CSP) is a rare but potentially life-threatening complication for women with 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 hemorrhage, shock, uterine rupture with potential hysterectomy, or even maternal death,³ and therefore should be diagnosed and effectively treated as early as possible. The incidence of CSP ranges from 1/2216 to 1/1800 in normal pregnancies,^{4, 5} and is likely to exponentially rise in the near future, due to an increasing rate of cesarean delivery worldwide and better detection by widespread use of transvaginal ultrasound.^{6, 7}

There have been several methods used in treating CSP. Options include conservative medical management, such as systemic or local administration of methotrexate (MTX), local administration of potassium chloride, hyperosmolar glucose, or crystalline trichosanin by hysteroscopy, laparoscopy or transvaginal ultrasound-guided injection. Surgical options include aspiration, dilatation and curettage (D&C), uterine artery embolization (UAE), hysteroscopy, myometrial wedge excision through laparotomy or laparoscopy, and hysterectomy.^{3,7,8} However, to date, there is no consensus on which is preferred. Here, we present our hospital's experience of 78 CSP cases, to promote awareness of the condition, as well as to offer a reference for its management.

PATIENTS AND METHODS

Patients

This study was a retrospective case series of 78 patients with a diagnosis of CSP treated there over a period of 4 years (January 2010 to December 2013). The medical records and ultrasound images of all patients with CSP were collected and reviewed. In all patients, the average age of the patients was 32.09 ± 4.80 (range 22-40) years. The average time between the current CSP and the previous cesarean delivery was 5.33 ± 3.64 (range 0.5-17.0) years. In terms of the number of cesarean deliveries before the CSP, 59 patients had 1, 18 patients had 2, and 1 patient had 3. The range of symptoms was wide. Of them, 52.56% (41/78) patients complained of intermittent slight vaginal bleeding, which in 9 cases was accompanied by hypogastralgia; 17.95% (14/78) patients suffered from excessive vaginal hemorrhage, of which 2 cases were spontaneous. Three patients (3/78, 3.85%) had only light abdominal discomfort, and 20 (20/78, 25.64%) were asymptomatic.

Diagnosis

Alongside a positive pregnancy test, CSP was confirmed by the following transvaginal ultrasound criteria^{9, 10}: (1) an

empty uterine cavity, without contact with the sac; (2) a clearly visible empty cervical canal, without contact with the sac; (3) 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) absent or diminished myometrial layer between the bladder and the sac (Fig. 1).

Cases were classified according to the two types of CSPs proposed by Vial *et al.*¹¹ The first type involves surface implantation: the trophoblast implants on the prior cesarean scar with growth towards the cervicoisthmus space or the uterine cavity. The second type is with deep implantation: there is implantation deep in the scar defect with growth towards the bladder and abdominal cavity. This second type is more prone to uterine rupture.

Treatment

The management strategies varied in individual cases depending on several criteria, including gestational age, severity of vaginal bleeding, sonographic findings, and level of serum β -human chorionic gonadotropin (β -hCG). All patients gave informed consent before treatment.

Curettage after UAE was performed with or without local MTX infusion. The uterine artery was selectively catheterized, with or without a 50 mg dose of MTX infused bilaterally. The bilateral uterine arteries were then embolized with 1-2 mm Gelfoam particles until the uterine arterial flow was lost (Fig. 2). Curettage was performed under the guidance of abdominal ultrasound 24-120 hours later. D&C was performed under the guidance of abdominal ultrasound by qualified doctors. For systemic MTX treatment (50 mg/m^2 body surface area), intramuscular injection was used, with a second dose one week later if necessary. For transvaginal sonogram guided local intragestational MTX injection, a 21-gauge needle was used (Hakko, Tokyo, Japan) under ultrasound guidance, the area of the gestational sac was identified for needle tip placement. A volume of 2-3 ml was first aspirated from the gestational



Figure 1. Transvaginal ultrasound images of a cesarean scar pregnancy at 7 postmenstrual weeks.

- A. Empty uterine cavity with gestational sac between cavity and cervix. EN: endometrium; GS: gestation sac.
- 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.

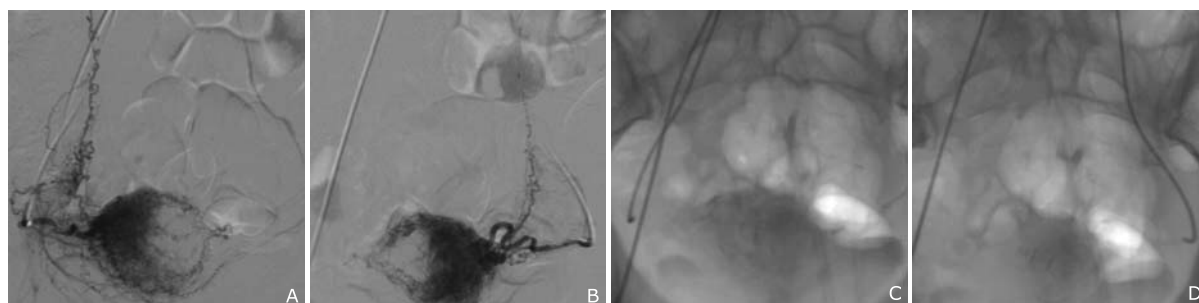


Figure 2. Uterine artery angiography before uterine artery embolization (A, B). Arterial embolization was confirmed after uterine artery embolization (C, D).

sac, and a 50 mg dose of MTX was then slowly injected. Laparotomies (hysterotomy, subtotal hysterectomy) were carried out by qualified gynecologists.

Outcome assessment and follow-up

The dynamic levels of serum β -hCG were determined every 3 days until the level had decreased by $>50\%$ from pre-therapy levels, then weekly until levels returned to normal. Ultrasound monitored the size of the gestational mass weekly until serum β -hCG had returned to normal levels, then monthly until the mass had disappeared.

The outcomes of patients' subsequent reproduction were recorded. Failure of the initial treatment was considered in the case of complications, such as massive vaginal bleeding (blood loss greater than 200 ml), when 7th day serum β -hCG continued to rise or decrease by $\leq 50\%$, or when the gestational mass became larger than pre-therapy levels. In these cases, additional therapies were given. All patients were asked not to have intercourse until the resolution of the CSP.

Statistical analysis

SPSS software version 19.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Continuous and ordinal data were presented as mean $\pm$ standard deviation, and categorical data were presented as the absolute count and percentage. The χ^2 test was used to compare the success rate between the laparotomy and emergency UAE. A P value <0.05 was considered statistically significant.

RESULTS

Among the 78 patients, 17 cases were first treated at our hospital. Two of them were initially misdiagnosed (one as threatened abortion, the other as incomplete abortion, and both had intermittent vaginal bleeding after conventional curettage was performed). The rate of misdiagnosis was 11.76% (2/17).

The remaining 61 patients were referred to us from

other hospitals. In 21 of these cases, the diagnosis of CSP was missed (2 were diagnosed with incomplete abortion, 18 as low intrauterine pregnancies, and 1 as inevitable abortion). Thirteen of these patients underwent D&C and 8 patients underwent medical abortion at other hospitals. The remaining 40 referred cases were initially diagnosed with or suspected to have CSP: 37 came to our hospital after diagnosis, and 3 came after failure of the medical abortion.

The clinical characteristics and findings of the treatments are presented in Table 1. Nine patients received successful laparotomies. Of them, 8 underwent hysterotomy (5 due to excessive hemorrhage), and 1 underwent subtotal hysterectomy because of massive bleeding and the patient's strong request, although the serum β -hCG level at that time was 190.3 U/L.

Fifty patients underwent curettage after UAE with or without local MTX infusion. This was successful in 42 (84%) cases. Four patients had severe vaginal bleeding during curettage and underwent hysterotomy. In four cases, treatments were considered failure. Three of them were given an additional transvaginal sonographic guided local MTX injection (50 mg) and later a second D&C. One patient underwent hysterotomy after extensive counseling.

Ten patients received D&C, and treatment failures occurred in four cases. Three underwent emergency UAE treatment to minimize massive vaginal bleeding and a second curettage was subsequently performed. Another patient was considered to be treated effectively and discharged, but 6 months later her serum β -hCG level remained abnormal and transvaginal sonographic revealed there was a remnant in the cesarean scar area. She went to Shanghai for a second curettage guided by ultrasound.

Six patients underwent transvaginal sonographic guided local intragestational MTX injection. Of these cases, three patients' treatment was considered a failure; one patient received an additional curettage and two patients received curettage after UAE. Three patients underwent systemic MTX injection, and two patients were treated with curettage after UAE after systemic MTX infusion developed treatment failure.

Table 1. Clinical characteristics and findings of the treatments

Items	Laparotomy	UAE	D&C	Local MTX	Systemic MTX
No. of cases	9	50	10	6	3
Serum β -HCG level [§] (U/L)	9270.87±6916.95	39779.58±44572.38	27392.99±19989.50	15248.05±18574.46	1017.03±1046.97
Gestational age [§] (d)	60.22±25.20	56.78±17.43	48.40±6.42	47.33±9.54	65.33±9.61
Diameter of the sac [§] (mm)	19.00±5.94	27.59±12.96	21.22±10.92	16.17±6.56	29.33±4.04
Deep implantations (%)	33.33 (3/9)	48.00 (24/50)	40.00 (4/10)	83.33 (5/6)	33.33 (1/3)
Success rate (%)	100.00 (9/9)	84.00 (42/50)	60.00 (6/10)	50.00 (3/6)	33.33 (2/3)
Hospitalization cost [§] (¥)	6327.36±2047.68	7815.41±2573.29	1884.88±1748.14	4306.37±3447.67	3651.67±3393.10
Time of recovery [§] (d)	25.00±14.77	35.49±15.60	39.89±16.41	33.83±7.57	56.33±20.60
Amount of bleeding [§] (ml)	97.78±43.81	81.04±174.56	30.50±20.61	38.33±20.21	53.33±5.77

§: Plus-minus values are means±SD.

UAE: curettage after uterine artery embolization with or without local methotrexate infusion; D&C: dilation and curettage; MTX: methotrexate; β -hCG: β -human chorionic gonadotropin.

There were 21 patients who had excessive vaginal hemorrhage, including 7 patients of documented failure who were initially treated in our hospital. Of these, 11 patients underwent emergency UAE treatment; 9 patients were successfully treated with laparotomy, and 1 patient received curettage with a balloon catheter inserted in the cervix and inflated to minimize blood loss for 24 hours. There was no significant difference in success rate between the laparotomy and emergency UAE [100% (9/9) vs. 81.82% (9/11), $\chi^2=0.289$, $P>0.05$].

During long-term follow-up, 18 patients were lost. There was one case of infertility who had been treated with curettage after UAE after the failure of transvaginal sonographic guided local intragestational MTX injection. The patient did not complain of any medication-associated side effects during treatment. Most patients required no further fertility-related interventions, as they no longer wished to conceive. Six cases conceived again and underwent induced abortion. One patient developed an ectopic pregnancy and received laparoscopic ipsilateral salpingectomy. There was no recurrence of CSP.

DISCUSSION

CSP is a rare form of ectopic pregnancy, and does not have any specific symptoms, so it can be easily mistaken for spontaneous miscarriage, low intrauterine pregnancy, cervical pregnancy, or trophoblastic tumor, and can lead to catastrophic complications.^{7, 12} Transvaginal ultrasound is considered the first-line diagnostic method of a potential CSP, since the examination is convenient, noninvasive, non-radioactive, and has a high diagnostic sensitivity.

However, approximately 15% of CSPs are misdiagnosed by transvaginal ultrasound alone.^{4, 13} Here, 11.77% (2/17) of patients who were first treated at our hospital were misdiagnosed by transvaginal ultrasound. Further, 21 of the 61 referred cases were misdiagnosed in other hospitals, and 10 of these patients suffered from excessive vaginal hemorrhage after or during D&C or medical abortion. Consequently, additional examinations like three-dimensional ultrasound, magnetic resonance imaging (MRI) are necessary to confirm difficult cases or when suspect the placenta is implanted.^{8, 14}

Because CSP can lead to serious complications, and because in the first trimester the embryo is soft and fragile, and the vascularity of the placental bed, the depth of placental implantation, and the risk of bladder invasion are considerably less than in later stages of pregnancy,¹⁵ CSP should be treated as early as possible when the diagnosis is confirmed. Traditional surgical options such as laparoscopic removal, excision of scar pregnancy on laparotomy, or hysterectomy are the most reliable ways to treat CSP and its complications. However, this procedure involves a large surgical wound, long hospital stay, and high hospitalization cost.^{3, 7, 16} Curettage after UAE with or without local MTX infusion is currently accepted as an effective treatment for CSP, and it is also usually used to control acute bleeding.^{15, 17} UAE has a number of advantages:¹⁸⁻²⁰ First, it blocks the blood supply of the gestational sac, which causes embryo ischemia, hypoxia, and finally atrophy and necrosis, while at the same time reducing the risk of bleeding during curettage. Second, in case of excessive bleeding, UAE can accurately detect and embolize the pelvic arteries to stop bleeding. Third, as an embolic agent, gelatin sponge can

embolize arteries effectively, but can be absorbed 14-21 days later, so that the blood flow of the uterus can recover and uterine function is not affected. Lastly, embolization combined with MTX infusion leads to the exposure of the embryo to a high local MTX concentration and causes the death of the trophoblast cells, while causing fewer side effects. As our study showed, curettage after UAE had a high success rate in the stable patients or patients suffered from excessive vaginal hemorrhage, and in patients suffered from excessive vaginal hemorrhage the success rate was no significant difference between UAE and laparotomy. What's more, as none had to undergo hysterectomy, and each patient's future fertility was preserved. So, curettage after UAE combined with or without local MTX infusion might be an effective and safe treatment for CSP.

In conclusion, CSP is becoming increasingly common, and is easily misdiagnosed and can lead to catastrophic consequences, so the correct diagnosis of CSP is of utmost importance. Curettage after UAE combined with or without local MTX infusion might be an effective and safe treatment for CSP, but there should be longer follow-up of these patients and further study is warranted in a larger patient population with CSP. In addition, awareness of CSP should start when a patient is discharged from the hospital after cesarean delivery; they should be advised to visit a doctor early for a transvaginal ultrasound in future pregnancies.

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