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*Full Length Research Paper*

# Treatment of cesarean scar pregnancy complicated with massive hemorrhage

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**The present study investigated suitable measures for treating cesarean scar pregnancy (CSP) complicated with massive hemorrhage. A total of 14 cases were diagnosed as CSP complicated with massive hemorrhage, and were treated from May 2003 to August 2009. Analyses of various factors related to hemorrhaging were carried out. According to the blood β-human chorionic gonadotropin (HCG) level, hemorrhaging onset time, ectopic pregnancy termination, etc., patients underwent uterine artery methotrexate (MTX) perfusion and uterine artery embolization (UAE), Foley's catheter uterine cavity compression and a protocol of MTX and leucovorin, or laparoscopic focal resection and uterine repair. There was no significant correlation between the hemorrhage quantity and hemorrhaging onset time, amenorrhea duration, β-HCG level, or ectopic mass size ($p > 0.05$). Hemorrhaging was promptly stopped, and all 14 patients were successfully cured without any case of intraoperative laparotomy or hysterectomy. Uterine artery MTX perfusion and UAE, Foley's catheter uterine cavity compression and MTX injection, as well as laparoscopic focal resection and uterine repair are all suitable options for treating CSP complicated with massive hemorrhage based on the specific conditions of the patient.**

**Key words:** Treatment, Cesarean section, scar, pregnancy, hemorrhage.

## INTRODUCTION

With the recent increase in the rate of Cesarean section deliveries, the incidence of Cesarean scar pregnancy (CSP) is also gradually rising (Aghamohammadi and Nooritajer, 2011; Michener and Dickinson, 2009; Jastrow et al., 2010). CSP, one of the delayed post-surgical maternal complications, is a type of ectopic pregnancy. Due to several factors (e.g., a weak myometrium, numerous connective tissues at the scar of the previous Cesarean section, aberrant development of decidua after pregnancy, and implantation of villus tissues into the myometrium at the time of the embedding of the gestational sac), an inadequate management such as medical abortion, curettage, or induced abortion without due caution cannot completely strip off villi or placental tissues promptly. The lower uterine section also cannot effectively constrict itself owing to lack of muscle fibers. Thus, once hemorrhaging occurs, it cannot be stopped, leading to serious and intractable massive hemorrhage (Zhuang et al., 2008; Hasegawa et al., 2009; Wanyonyi and Karuga, 2010).

The biggest threat of CSP is its association with the complication of massive focal hemorrhaging, which may consequently lead to uterine resection, or even worse, death. Thus, the effective management of hemorrhaging caused by CSP has recently become a core issue in treating patients with CSP. Based on clinical analyses of the treatment of 14 patients suffering from CSP with massive hemorrhage, the present study explored plausible treatment measures for the complication.

## MATERIALS AND METHODS

### Clinical data

Between May 2003 and August 2009, 41 CSP patients were treated in Yuyao People's Hospital, China. Single vaginal hemorrhage quantity ≥ 400 ml was found in 14 cases (34.1%). The current research was approved by the local ethics committee of the Yuyao People's Hospital, China, and conformed to the provisions of the declaration of Helsinki (as revised in Tokyo in 2004).

For the 14 cases, the ages ranged from 20 to 45 (average =

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**Table 1.** Comparisons of the duration of amenorrhea, the blood level of β-HCG and the size of the ectopic mass among different groups with different hemorrhage quantities ($\bar{X} \pm S$).

| Hemorrhage quantity (ml) | N | The duration of amenorrhea (days) | β-HCG(IU/L) | Size of the mass (cm) |
|---|---|---|---|---|
| 400 ~ | 7 | 64 ± 17 | 18086 ± 14235 | 3.9 ± 1.8 |
| 800 ~ | 4 | 85 ± 26 | 33841 ± 25796 | 4.1 ± 1.4 |
| 1200 ~ | 3 | 88 ± 25 | 38340 ± 20162 | 4.6 ± 0.7 |
| F value | | 3.807 | 0.171 | 0.335 |
| P value | | 0.077 | 0.687 | 0.574 |

29.6). The gravidities (including that during the study) were 3 to 8 (average = 5.1). The parities were 1 to 2 (average = 1.36). The durations of amenorrhea were 45 to 112 days (80 ± 28 days). The time spans from the previous Cesarean section were 0.75 to 7 years (average = 2.94 years). The blood pressures while hemorrhaging were 70/40 to 110/70 mmHg (average = 94.5/58.5 mmHg; 1 mmHg = 0.133 kPa). The blood levels of β-human chorionic gonadotropin (HCG) were 591 IU/L to 106 639 IU/L (20 501 ± 18 793 IU/L).

#### Hemorrhaging onset time and single hemorrhage quantity

Among the 14 cases, 11 were emergency admissions due to massive vaginal hemorrhage. Among these 11 admissions, 7 hemorrhaged after medical termination of misdiagnosed early pregnancy (including 3 that occurred during uterine clearing after medical termination), 2 hemorrhaged after induced abortion during midtrimester pregnancy (14 and 16 weeks), and 2 hemorrhaged after pregnancy. The hemorrhage quantities ranged from 400 to 1500 ml (878 ± 479 ml) by visual measurement. The remaining 3 patients presented massive vaginal hemorrhage during an embryo-killing treatment based on a protocol of methotrexate (MTX) + leucovorin (cf) at the hospital. The hemorrhage quantities ranged from 400 to 1000 ml (750 ± 353 ml) measured by the volumetric method.

#### Ultrasonic diagnoses and criteria

The diagnoses of 11 cases with massive hemorrhage emergency were made using a portable color doppler transvaginal ultrasound scanner under asepsis. The remaining three were routinely diagnosed using a color doppler transvaginal ultrasound scanner. The transvaginal ultrasonic diagnosis criteria used in the current study were the CSP ultrasonic diagnosis criteria initially established by godin et al. (1997), combined with recent updates concerning CSP ultrasonography reported in literature (ash et al., 2007). The criteria were as follows: (1) no gestational sac in the uterine cavity or cervical canal, (2) the gestational sac or the mass was located at the cervical inner introitus in the anterior wall of the isthmic portion or at the scar of the previous cesarean section, (3) the myometrium between the posterior wall of the bladder and the sac or the mass was thin or possessed a defect, (4) low-resistance and high-speed circular blood flow signals were detected around the sac trophoblast by color doppler flow imaging, and (5) no mass detected around the adnexal areas. After ultrasound examination, all 14 patients met all the aforementioned criteria. The myometrium thickness between the bladder and sac or mass, fell within the range of 2 to 5 mm with an average of 3.1 mm. The diameter of the sac or mass was from 2.4 to 7.9 cm (4.2 ± 1.4 cm).

#### Treatment methods

Along with combined methods, such as volume expansion and counter-shock therapies, 7 patients (including 3 presenting massive hemorrhage after medical abortion with β-HCG ≥ 5000 IU/L, 2 after induced abortion in the second trimester, and 2 after pregnancy) took emergent uterine artery MTX perfusion (100 to 300 mg) and underwent uterine artery embolization (UAE). Four patients presenting massive hemorrhage after medical abortion with β-HCG < 5000 IU/L took a protocol of MTX + CF and underwent Foley's catheter uterine cavity compression (Floridon et al., 1996; Krag et al., 2009). The Foley's catheter uterine cavity compression was conducted by inserting a 16 to 18 f urinary catheter (Shida Company, Zhanjiang) into the uterine cavity, and then injecting 20 to 30 ml normal saline into the foam rubber balloon to form a water bag. By appropriately dragging the end of the catheter, the water bag was kept blocked by the cervical inner introitus to compress the hemorrhagic foci in the anterior wall of the isthmus uteri. After hemorrhaging was stopped by 24 to 48 h of compression, the catheter was taken out. All aforementioned 11 patients underwent curettage under hysteroscopic guidance when the β-HCG level decreased from 80 to 90%, and hemorrhaging totally or almost disappeared. The other 3 patients who presented massive hemorrhage during embryo-killing treatment underwent laparoscopic focal resection and uterine repair (Ben et al., 2007; Leite et al., 2009).

#### Statistical analysis

The SPSS 13.0 software was used for statistical analyses. One-way ANOVA and the *t*-test were employed to compare measurement data. $p < 0.05$ was considered as statistically significant.

## RESULTS

### Hemorrhaging onset time and single hemorrhage quantity

According to different onset times of hemorrhaging, the patients were divided into two groups, namely, the group that hemorrhaged before hospital admission ($n = 11$), and the group that hemorrhaged during the embryo-killing treatment ($n = 3$). By comparing their different single hemorrhage quantities (878 ± 479 to 750 ± 353 ml, respectively), the result was $t = -0.339$ ($p = 0.740$), which showed no statistical significance. The correlations of the hemorrhage quantity with the duration of amenorrhea,

blood level of β-HCG, or size of ectopic mass are shown in Table 1. The duration of amenorrhea, β-HCG level and size of ectopic mass all increased with increased hemorrhage quantity, but the differences had no statistical significance.

### Treatment outcomes

The hemorrhaging of the seven patients that underwent uterine artery MTX perfusion (100 to 300 mg) and UAE was promptly and effectively controlled. Between 6 and 19 days (10 ± 5 days) after treatment the patients underwent curettage under hysteroscopic guidance with an intraoperative hemorrhage quantity of 65 ± 47 ml and an operative time lasting of 17 ± 9 min. The hemorrhaging of the four patients that underwent Foley's catheter uterine cavity compression and a protocol of MTX + CF was stopped within 1 to 2 days. The patients underwent curettage under hysteroscopic guidance 4 to 14 days (9 ± 4 days) after the treatment with an intraoperative hemorrhage quantity of 59 ± 37 ml and an operative time lasting 16 ± 8 min. The hemorrhaging of the three patients that underwent laparoscopic focal resection and uterine repair was promptly stopped after the operation. The operative time lasted from 45 to 68 min, and the intraoperative hemorrhage quantity was from 80 to 360 ml. All patients were successfully cured and discharged from the hospital without any case of intraoperative laparotomy or hysterectomy. The patients that underwent endovascular interventional therapy did not present serious syndromes after embolism or MTX toxicity reactions.

### Pathological findings

The focal tissue samples of the 14 patients were identified as degenerate, necrotic fetal villi or placental tissues by pathological inspections.

## DISCUSSION

We demonstrated that one-third of CSP patients suffer from the complication of massive hemorrhage. CSP complicated with massive hemorrhage has become a severe emergency in gynecology and obstetrics, and it poses one of the biggest health risks to young women who have undergone a cesarean section delivery (alderdice et al., 2003; bashiri et al., 2008; yang et al., 2010; lu et al., 2011). Therefore, the effective management of massive hemorrhage induced by CSP has gained increasing attention in gynecology and obstetrics.

The results of the present study show that the difference between hemorrhage quantities at different times is not statistically significant ($p > 0.05$). This finding indicates that the hemorrhage quantity has no apparent correlation with the hemorrhaging onset time, duration of amenorrhea, blood level of β-HCG, and size of the ectopic mass ($p > 0.05$). Therefore, predicting the hemorrhaging onset time of a CSP patient and detecting the risk factors normally related to hemorrhaging are difficult. The exceptions are conditions in which the following inadequate iatrogenic interventions are performed: medical or induced abortion and curettage due to misdiagnosed intrauterine early pregnancy; induction of labor in midpregnancy because of an erroneous normal pregnancy diagnosis without type-b ultrasonic placental localization before operation, or due to a localization mistake; and curettage during hospitalization when the embryo has not yet been killed or when the focal blood flow is still abundant. Obviously, the selection of a suitable protocol (uterine artery MTX and UAE, Foley's catheter uterine cavity compression and a protocol of MTX + CF, laparoscopic focal resection and uterine repair, etc.) according to specific patient conditions (blood level of β-HCG, hemorrhaging onset time, ectopic pregnancy termination, etc) is very important for the management of CSP complicated with massive hemorrhage.

In the present study, uterine artery MTX perfusion and UAE were decisively adopted to kill the embryo and stop the hemorrhage for the emergency admission patients with relatively higher β-HCG levels (the normal level is 5000 IU/L), massive hemorrhage after induction of labor in the second trimester, or spontaneous hemorrhaging after pregnancy. Compared with total administration, uterine artery MTX perfusion has several unparalleled advantages. In recent years, uterine artery MTX perfusion has been found as being able to enter the pregnancy foci directly and quickly and remaining there. Consequently, the consumption of the maximum dose of MTX by the focal tissues is ensured. The obtained drug concentration can be increased 2 to 22 times with a much lower protein-binding rate, which apparently increases the amount of bioactive free drug. As a result, drug efficacy can be increased 4 to 10 times with a significantly promoted embryo-killing capacity (xu et al., 2007). A single MTX dose for uterine artery perfusion is not restricted by weight or body surface area (the restricted single dose for total administration is 1 mg/kg or 50 $mg/m^2$, respectively). In the present study, the maximum single dose of MTX used was 300 mg, which does not lead to serious drug toxicity reactions. UAE was carried out after uterine artery MTX perfusion. UAE can reduce the uterine artery pressure and reduce the speed of blood flow to form a thrombus. The thrombus can degenerate and necrotize the pregnancy foci sensitive to ischemia-hypoxia by blocking the blood supply to accelerate embryonic death. UAE can also prolong the MTX residence and treatment time in foci to increase the treatment effectiveness by reducing the blood flow speed

in the uterine artery. UAE can quickly control focal hemorrhaging, and also plays a protective role in the subsequent curettage. Thus, UAE decreases the risk of intraoperative hemorrhaging. In the present study, the hemorrhaging of the seven patients that underwent uterine artery MTX perfusion and UAE was promptly controlled, and the embryos were effectively killed. This result indicates that uterine artery MTX perfusion and UAE can be used as a major treatment procedure for CSP patients complicated with massive hemorrhage.

For the patients with β-HCG levels <5000 IU/L after medical abortion, the total MTX administration dose can be used in the embryo-killing treatment. However, the prompt and effective control of massive hemorrhage is also necessary. Foley's catheter uterine cavity compression is a convenient, safe, and effective method for stopping hemorrhage (Ahmed et al., 2010; Ben et al., 2007; Al-nazer et al., 2009). The soft and flexible water bag, which is formed by injecting water into the foam rubber balloon, is disposed to fit the shape of the uterine cavity. It can evenly and tightly compress the hemorrhaging foci by appropriate dragging. Consequently, the blood sinusoid is effectively compressed and closed off. After local thrombi are formed and hemorrhaging is stopped, the catheter can be taken out. Normally, hemorrhaging can be stopped after 24 to 48 h of compression. Apart from stopping hemorrhage, the apical opening of the catheter can drain the hematocele in the uterine cavity for the convenience of hemorrhaging observation. In the current work, the outcomes of the hemorrhaging-stopping treatment of four patients proved that Foley's catheter uterine cavity compression is an effective measure to stop hemorrhaging.

For the CSP patients presenting massive hemorrhage during hospitalization, an effective radical treatment method is urgently needed after the proper procedures for hemostasis and embryo-killing have been performed. Laparoscopic operation can result in the prompt and effective clearing of pregnancy focal tissues, as well as simultaneously suturing up rifts and repairing uterine defects to preserve the pregnancy ability of the patient. Thus, laparoscopic operation is a safe and effective radical treatment method especially for patients with a deeply implanted scar or pregnancy foci extending to the abdominal cavity or bladder (Wang et al., 2005; Lee et al., 1999).

The outcomes of the treatment of three patients in the present study prove that laparoscopic focal resectioning and uterine repair is an effective method for hemostasis and radical treatment. However, the surgery requires skillful operational techniques; caution is warranted against residual foci and incomplete rift suturation, which can lead to rehemorrhaging.

In the present study, 11 patients underwent curettage under hysteroscopic guidance after UAE or Foley's catheter uterine cavity compression. These procedures are similar to those performed unassisted by a hysteroscope, but have the advantages of accurate localization, guided operation, shorter operative time, less intraoperative hemorrhage, and increased focus clearance (Cheng et al., 2007). Using this technique as the major method for CSP focal clearing in our hospital, relatively satisfying treatment outcomes are obtained.The outcomes obtained in the current study also prove its efficacy.

Among 30 non-emergency cases admitted in our hospital, obvious hemorrhaging were not present in 27 cases (90%) during embryo-killing treatment, and uteri were successfully preserved. These results suggest that for these non-emergency CSP patients, different treatment protocols such as conservative MTX treatment, intra-arterial treatment, and/or surgical treatment (including normal hysteroscopic curettage, transabdominal, or laparoscopic focal resection with uterine repair) should be selected according to various specific conditions (the blood level of β-HCG, focal size, degree of blood flow, vaginal hemorrhaging, and therapeutic measures performed outside the hospital). Curettage should be carried out when the β-HCG level is decreased by 80 to 90% and the focal blood flow totally or almost disappears.

In conclusion, uterine artery MTX perfusion and UAE, Foley's catheter uterine cavity compression and MTX injection, together with laparoscopic focal resection and uterine repair are all suitable options for treating CSP complicated with massive hemorrhage.

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