Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 489–492

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Management of type II unruptured cesarean scar pregnancy: Comparison of gestational mass excision and uterine artery embolization combined with methotrexate

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ARTICLE INFO

Article history:
Accepted 15 January 2014

Keywords:
cesarean scar pregnancy
laparotomy
uterine artery embolization

ABSTRACT

Objective: This research was carried out to investigate the effectiveness, rationality, and safety of laparotomy management compared with uterine artery embolization (UAE) combined with methotrexate (MTX) for the treatment of deep implantation cesarean scar pregnancy (CSP II).

Materials and methods: Data from 29 patients seen between June 2008 and February 2012 were retrospectively analyzed. The patients were divided into the surgery group and the UAE combined with MTX group according to the treatment they received. We compared the clinical characteristics and treatment outcomes between the two groups.

Results: The patients' clinical characteristics did not differ between the surgery group and the UAE combined with MTX group. However, the mean blood loss was decreased in the surgery group compared with the UAE combined with MTX group (90 ± 4.5 mL vs. 286 ± 5.2 mL, $p < 0.05$). No patients required blood transfusion in the surgery group, whereas two patients in the UAE combined with MTX group received blood transfusions. The length of time for the serum beta human chorionic gonadotropin (β-HCG) level to normalize, the time required for the disappearance of the gestational mass, and the duration of hospital stay were significantly less in the surgery group than in the UAE combined with MTX group (13.7 ± 1.0 days vs. 40.7 ± 1.7 days, 7.1 ± 1.3 days vs. 135.4 ± 6.7 days, and 11.0 ± 1.2 days vs. 41.4 ± 3.2 days, respectively; $p < 0.01$). Although the treatment success rate did not differ significantly between the two groups, the success rate was 100% for the surgery group and 73% for the UAE combined with MTX group.

Conclusion: Surgical treatment can remove gestational masses and allow wound repair. Moreover, laparotomy is available in almost all hospitals. Thus, surgery can be an effective and reasonable treatment for CSP II.

Introduction

Cesarean scar pregnancy (CSP) is a rare but very dangerous form of ectopic pregnancy, characterized by the embryo invading the myometrium of a previous cesarean scar [1,2]. Patients with CSP face a high risk of uterine rupture, severe bleeding, hysterectomy, and fertility loss. The reported incidence of CSP is approximately 1:1800–1:2216 of all cesarean deliveries and accounts for 6% of ectopic pregnancies among women who have previously had a cesarean delivery [3,4]. In recent years, the cesarean delivery rate has increased worldwide, which has contributed to a rise in CSP [5].

Vial et al [6] defined two types of CSP. CSP I refers to the implantation of the gestational sac on a previous cesarean scar with progression in the cervico-isthmus and the uterine cavity. CSP II refers to a deep implantation of the amniotic sac in a cesarean scar defect with progression towards the myometrium and the uterine serosal layer. In CSP II cases, the thickness of the uterine myometrium between the gestational sac and the bladder wall is usually less than 4 mm. Although the former condition may result in a viable birth, the latter condition has an increased risk of life-threatening bleeding and uterine rupture during the first

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http://dx.doi.org/10.1016/j.tjog.2015.08.002

trimester. Thus, once CSP II is considered, immediate treatment is warranted.

Several treatment options have been reported, including excision of the gestational sac by laparotomy or laparoscopy, uterine artery embolization (UAE), medical treatment, and dilation and curettage. However, there is currently no consensus on the optimal management for CSP, especially CSP II. In this article, we analyze the different treatment methods for CSP II patients, including excision of the gestational sac by laparotomy and by UAE combined with methotrexate (MTX), and discuss the feasibility and rationality of different management options.

Materials and methods

Patients

Our study was approved by the ethics committee of Shanghai Jiaotong University. Data from 29 patients diagnosed with CSP II in Shanghai Jiaotong University Affiliated Shanghai First People's Hospital between June 2008 and February 2012 were retrospectively evaluated. All patients had a history of previous cesarean delivery. The diagnosis of CSP II was made with a positive pregnancy test and transvaginal sonography. According to the literature [2,7,8], the ultrasound diagnostic criteria are the following: no evidence of gestation found in the uterine cavity or endocervical canal; the gestational sac is implanted in the anterior isthmic wall of the uterus; a thin or absent myometrial layer is present between the gestational sac and the bladder; and color power Doppler images show a hypervascular signal in the cesarean scar area.

Treatment methods

The patients were divided into two groups according to the management method used: 14 patients underwent surgery (surgery group) and 15 patients underwent UAE combined with MTX (UAE combined with MTX group). In the surgery group, the patients underwent excision of the gestational mass and scar repair by laparotomy.

UAE was performed by an experienced radiologist. After the left or right femoral artery was successfully punctured, a 5F Roberts uterine catheter was superselectively inserted into the bilateral uterine arteries, and 100 mg of MTX was infused bilaterally via the uterine catheter. Once the blood flow slowed, gelatin sponge particles were used to block the uterine arteries until blood flow was occluded. Angiography was performed to confirm embolization. The serum beta human chorionic gonadotropin (β-HCG) level was monitored weekly following UAE. If the β-HCG level dropped by less than 50%, the patients received a 1 mg/kg dose of MTX intramuscularly.

Evaluation of results

Serum β-HCG measurements and color transvaginal sonography examinations were performed weekly. The clearance time of serum β-HCG, the clearance time of the gestational mass as verified by transvaginal sonography, amount of hemorrhage, duration of the hospital stay, failure rate of the treatment, side effects, and complications were recorded. An outcome of failure was defined as massive hemorrhage (>500 mL), continuous or plateau serum β-HCG levels, or the need for a hysterectomy.

Statistical analysis

SPSS 11.0 software was used for the statistical analysis, and the data were expressed as the means ± standard deviation. The nonparametric Mann–Whitney test was used to compare the blood loss, time for serum β-HCG to return to normal, time for the gestational mass to resolve, and duration of hospital stay. Fisher's exact test was used to compare the success rates. All p values <0.05 were considered significant.

Results

Clinical characteristics

All of the patients presented with amenorrhea. In addition, 25 patients reported a small amount of vaginal bleeding, 21 complained of low abdominal pain or low back pain, and five presented with isolated amenorrhea. The physical examination showed that the uterus was of nongravid size or the size of a 6-week gestation pregnancy in all patients. The serum β-HCG level was increased in all patients. All of the patients met the diagnostic criteria for CSP II. The mean age, mean parity, number of previous cesarean deliveries, duration since last cesarean delivery, gestational sac diameter, thickness of the anterior lower uterine segment myometrium, and gestational age are displayed in Table 1.

Comparison of blood loss and success rate between the surgery group and the UAE combined with MTX group

Fourteen patients underwent excision of the gestational mass and wound repair by laparotomy. In all cases, the fallopian tubes and ovaries appeared normal; however, we observed a blue-tinted gestational sac located in the previous cesarean scar and protruding into the uterine serosal surface. The anterior uterus myometrial wall was very thin or absent. No blood was found in the abdominal cavities of the patients, and the mean blood loss for patients who underwent surgery was 90 ± 4.5 mL (range 40–150 mL). Fifteen patients were treated with UAE combined with MTX, and all received MTX intramuscularly (weekly for 2–3 weeks) because the serum β-HCG level failed to decrease. Severe vaginal bleeding

Table 1
Clinical characteristics of patients with CSP II.

Characteristics	Surgery group (n = 14)	UAE combined with MTX group (n = 15)	p
Age (y)	31.1 ± 1.8	31.7 ± 1.7	0.82
Number of previous cesarean deliveries	1.2 ± 0.1	1.1 ± 0.1	0.74
Time since last cesarean delivery (y)	2.4 ± 0.3	1.9 ± 0.2	0.61
Gestational age (d)	47.1 ± 3.8	43.7 ± 1.4	0.34
Diameter of gestational sac (mm)	30.5 ± 1.2	31.3 ± 1.1	0.52
Thickness of anterior lower uterine segment myometrium (mm)	2.5 ± 0.6	2.7 ± 0.4	0.23
Serum β-HCG level (mIU/mL)	8776 ± 235	8302 ± 367	0.35

Data are presented as mean ± standard deviation.
β-HCG = beta human chorionic gonadotropin; CSP = cesarean scar pregnancy; MTX = methotrexate; UAE = uterine artery embolization.

Table 2
Comparison of blood loss and success rate in the surgery and UAE groups.

	Surgery group ($n = 14$)	UAE combined with MTX group ($n = 15$)	p
Blood loss (mL), mean ± SD	90 ± 4.5	286 ± 5.2 mL	<0.05
Success rate (%)	14/14 (100%)	11/15 (73%)	>0.05

MTX = methotrexate; SD = standard deviation; UAE = uterine artery embolization.

(300 mL on each occasion) occurred repeatedly in four patients after UAE combined with MTX. These four patients underwent emergency laparotomy for excision of the gestational mass. Two of those patients received a blood transfusion because of excessive blood loss. The patients managed with UAE combined with MTX had a mean blood loss of 286 ± 5.2 mL (range 130–1000 mL). No patient in either group underwent a hysterectomy. As shown in Table 2, the blood loss in the surgery group was less than in the UAE combined with MTX group ($p < 0.05$). The success rate was 100% in the surgery group and 73% in the UAE group, although this difference was not significant.

Comparison of clinical characteristics after the treatment and duration of hospital stay

The serum β-HCG level returned to normal within 13.7 ± 1.0 days postoperatively in patients who underwent surgery (range 10–18 days). The mean period for the serum β-HCG level to return to normal was 40.7 ± 1.7 days (range 30–55 days) in patients treated with UAE combined with MTX ($p < 0.05$; Table 3).

Patients in the surgery group were examined by transvaginal ultrasound 7 days (mean 7.1 ± 1.3 days) postoperatively, with no intrauterine mass identified. Patients in the UAE combined with MTX group were monitored by weekly transvaginal ultrasound after the treatment until the serum β-HCG was negative, and the intrauterine masses in these patients disappeared from 90 to 180 days after the procedure (mean 135.4 ± 6.7 days; Table 3).

As shown in Table 3, the mean duration of hospital stay was 9.0 ± 1.2 days (range 7–15 days) in patients who underwent surgery and 41.4 ± 3.2 days (range 34–64 days) in patients treated with UAE combined with MTX ($p < 0.01$).

Comparison of complications between the two groups

Patients who underwent surgery did not suffer any complications. Vaginal bleeding stopped 7–10 days postoperatively. The most common complications in patients treated with UAE combined with MTX included lower abdominal pain (8/15), fever (5/15), and nausea and vomiting (4/17). All patients in the UAE combined with MTX group had more than 30 days of vaginal bleeding, and three patients presented with infection and were treated with antibiotics.

Discussion

CSP is a rare but life-threatening type of ectopic pregnancy and should be treated as quickly as possible after its diagnosis. Generally, termination of the pregnancy in the first trimester is recommended. Treatment options for CSP include medical treatment, surgery, UAE, or a combination of these methods; however, the optimal treatment is not yet known. Management should be personalized to the patient with consideration for the CSP type, gestational age, future fertility, and gestational viability [9].

CSP II presents a greater treatment challenge than CSP I. UAE was initially adopted as a treatment for gynecologic and obstetric hemorrhage conditions, such as postpartum hemorrhage, uterine myoma, and cervical pregnancy. Recently, UAE has gained wide acceptance as a treatment for CSP [10,11], and MTX has been reported as an alternative treatment for CSP but with a high failure rate. The administration of intravascular MTX prior to occlusion facilitates a high MTX concentration in the CSP mass with less toxicity and fewer adverse effects compared with systemic MTX administration [12]. UAE combined with MTX not only blocks the blood flow to the CSP but also has a direct embryocidic effect. This combination has been an effective method for the treatment of CSP [13]. Zhang et al [14] reported that 11 patients with CSP underwent UAE combined with MTX followed by uterine curettage, resulting in the successful treatment of 10 patients. However, uncontrolled hemorrhage occurred during curettage in one patient, and open surgical excision of the low segment of the uterus was performed. The authors suggested that UAE combined with MTX followed by uterine curettage might be an effective and safe method to treat CSP. Takeda et al [15] described UAE as an initial conservative method used for five CSP cases with total or subtotal placental invasion to the anterior uterine wall. Additional MTX, hysteroscopic resection, or MTX plus hysteroscopic removal were administered in four cases, and spontaneous expulsion of gestational products occurred in one case. The authors posited that CSP with deep placental invasion to the anterior uterine wall is difficult to manage conservatively, and that additional medical and/or surgical measures should be individually used. Our study demonstrated that all CSP II patients treated with UAE combined with MTX required systemic MTX application, with four of 15 patients suffering from severe bleeding. Our findings suggest that UAE combined with MTX is not a good option for the treatment of CSP II.

Laparotomy is available in all hospitals and is effective for the removal of the gestational mass and scar repair. If uterine scar dehiscence accompanies cesarean scar implantation, potentially affecting future pregnancies, only surgical resection offers the opportunity to remove the pregnancy and simultaneously repair the defect, restoring the potential for successful subsequent pregnancies [13,16]. Resection of the old scar and the new closure can minimize the risk of recurrence [6].

Table 3
Comparison of characteristics after the treatment and duration of hospital stay.

	Surgery group ($n = 14$)	UAE combined with MTX group ($n = 15$)	p
The time for serum β-HCG level to return to normal (d)	13.7 ± 1.0	40.7 ± 1.7	<0.01
The time required for gestational mass disappearance (d)	7.1 ± 1.3	135.4 ± 6.7	<0.01
Duration of hospital stay (d)	11.0 ± 1.2	41.4 ± 3.2	<0.01

β-HCG = beta human chorionic gonadotropin; MTX = methotrexate; UAE = uterine artery embolization.

Our study compared UAE combined with MTX with surgery for the treatment of CSP. We found that the mean blood loss, duration of hospital stay, and time for serum β-HCG level to return to normal were less in the surgery group than in the UAE combined with MTX group. Although there was no significant difference in the success rates between the two groups, the surgery group success rate was 100%, whereas the UAE group success rate was 73%. Our study showed that if UAE combined with MTX was performed as an initial treatment for CSP patients with deep invasion to the uterine wall, all the patients would require further treatment, which could increase the cost of treatment, duration of hospital stay, and risk of complications.

For patients with stable hemodynamics, the treatment aims to excise the gestational mass and preserve future fertility. Simultaneous resection of the scar with the gestational mass and wound repair is a feasible method to treat CSP. This method can repair the wound in addition to terminating the pregnancy, decreasing the risk of recurrence, and preserving future fertility. However, some researchers believe that laparotomy can increase postoperative adhesions and affect fertility [6].

Laparoscopy is a minimally invasive procedure for CSP and can remove gestational tissue and allow for wound repair. The first CSP case successfully treated by laparoscopy was reported in 1999 [17], with several other successful cases reported since then. Laparoscopy can confirm the diagnosis, remove the gestational products, and repair the uterine defect. Some researchers have suggested that laparoscopy may be a reasonable alternative to laparotomy for an unruptured CSP [18]. Recently, Wang et al [19] reported that 11 patients with CSP II were successfully managed by laparoscopy or by laparoscopy combined with a transvaginal approach. In their study, the average operative time was 85.5 ± 17.5 minutes, and the mean blood loss was 250.0 ± 221.4 mL. The serum β-HCG level returned to <100 mIU/mL within 16.4 ± 5.3 days postoperatively. Thus, in hospitals that offer laparoscopy, laparoscopic CS resection with wound repair is a safe and effective treatment for CSP II, especially after the failure of medical treatment.

In conclusion, our study suggests that resection of the gestational mass and wound repair is a safe and effective treatment for CSP II. Our findings are limited by our small retrospective study design. Further randomized cohort studies are warranted to elucidate the optimal treatment for CSP II.

Conflicts of interest

The authors report no conflicts of interest.

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