Clinical characteristics and salvage management of persistent cesarean scar pregnancy

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Abstract

Aim: The study was conducted to illustrate the clinical characteristics and treatment outcomes of patients with persistent cesarean scar pregnancy (PCSP).

Methods: During a six-year period, 38 cases of PCSP were diagnosed and treated conservatively to preserve fertility. The clinical presentations, imaging findings and treatment outcomes of these patients were reviewed.

Results: Fourteen out of 38 women (37%) presenting with PCSP suffered heavy vaginal bleeding. Gestational age at diagnosis was 73.1 ± 21.7 days. The maximum diameter of the PCSP mass was 3.6 ± 1.6 cm. The presence of a rich vascular pattern in the area of the PCSP mass was detected by ultrasound in 33/38 (87%) patients. Six patients with a PCSP gestational age of 64.2 ± 6.2 days and a mass diameter of 2.5 ± 0.6 cm were successfully treated with medical treatment alone and 32 patients with a gestational age of 74.8 ± 23.1 days and a mass diameter of 3.8 ± 1.6 cm were successfully treated with surgical or combined treatment.

Conclusions: Patients with PCSP are diagnosed at advanced gestational age and are more prone to heavy bleeding. Surgery is the main treatment for PCSP. Medical treatment of PCSP has become an attractive alternative, especially for hemodynamically stable patients with a PCSP mass with a maximum diameter of < 3.5 cm.

Key words: cesarean scar pregnancy, cesarean section, ectopic pregnancy, hemorrhage, persistent ectopic pregnancy.

Introduction

Cesarean scar pregnancy (CSP) is a rare type of ectopic pregnancy in which the embryo is implanted in a scar from a previous cesarean section.1,2 CSP incidence is increasing worldwide, especially in China.3 This is possibly because of the increase in cesarean delivery rates and the wide use of transvaginal color Doppler ultrasound as a diagnostic method.1,4,5 CSP is associated with severe complications, such as life-threatening bleeding and uterine rupture.6,7 Early diagnosis and timely termination of the pregnancy in the first trimester are strongly recommended for the management of CSP.1,8

First-line treatment for CSP has not yet been established. Although many methods have been reported, transvaginal surgical evacuation under ultrasound or hysteroscopy guidance has been widely adopted in China.9–12 Previous studies have confirmed the clinical efficacy and safety of transvaginal surgical evacuation.13 However, persistent remains of an ectopic pregnancy mass after surgical evacuation (described as residual gestational tissue), retained products of conception or pregnancy remnants have also been reported.12–14 The term “persistent cesarean scar pregnancy” originated with a 2012 case series by Zhang et al. and was used to diagnose CSP with the persistent remains of an ectopic pregnancy mass after surgical evacuation.
evacuation. The objectives of our study were to illustrate the clinical features and to share our experience of the management of patients with PCSP.

Methods

This retrospective study was conducted in a tertiary university affiliated hospital. The Ethics Committee of Women’s Hospital, Zhejiang University School of Medicine, China, approved the study protocol. Our hospital is the largest obstetric and gynecological unit in Zhejiang Province and many obstinate diseases (including CSP) are referred to our hospital. The medical records of all patients who were diagnosed with CSP between January 2010 and May 2016 were reviewed. The diagnostic criteria for CSP are as follows: a history of cesarean section in the lower uterine segment; positive serum β-human chorionic gonadotropin (β-hCG) levels; and fulfillment of the following ultrasound standards: no fetal parts in the uterine cavity or cervix, development of the gestational sac in the anterior portion of the lower uterine segment, a thin myometrial layer between the gestational sac/placenta and bladder and the presence of a rich vascular pattern in the area of the cesarean scar and the placenta. Patients were initially offered a choice between medical or surgical treatment. The data of patients with CSP treated by surgical evacuation under ultrasound or hysteroscopy guidance was reviewed. Pathological examination of all patients confirmed the presence of chorionic villus or trophoblast cells. Thirty-eight women who had been followed-up manifested a persistent or growing ectopic pregnancy mass at the site of the cesarean section with or without the plateau or rebound of serum β-hCG level. All of these women were all diagnosed with PCSP and were enrolled in our study.

Patients with PCSP were informed about the poor understanding and limited clinical experience of treatment for PCSP. The choice of treatment modality was determined after full discussion between patients and doctors. Final decisions were made depending on patients’ clinical symptoms and preferences, experience from prior treatments and the capabilities of the doctors and reference to current literature regarding treatment for CSP or PCSP. All of the patients wanted to preserve their fertility. Women who did not experience heavy vaginal bleeding were considered eligible for both medical and surgical management options. Women who were not eligible or were unwilling to undergo further surgery were offered medical treatment, which mainly involved a single-dose intramuscular injection of methotrexate (MTX, 50 mg/m² body surface area). Failed medical treatment and heavy bleeding were indications for surgical treatment. Surgery mainly involved repeat surgical evacuation and resection of the PCSP mass. Surgical evacuation was performed under ultrasound or hysteroscopy guidance. Heavy intraoperative uterine bleeding was conservatively managed by vaginal gauze packing. Resection of the lesion and repair of the uterine defect by laparoscopy or laparotomy were recommended for patients with an exogenous PCSP mass.

All women were followed up twice a month for the first month, and once a month in the following months if necessary. Follow up included measuring the serum β-hCG level and an ultrasound examination. A successful outcome was defined as the normalization of serum β-hCG levels, disappearance of the PCSP mass and avoidance of major complications (hemodynamic instability, uterine scar rupture and hysterectomy).

Statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, NY, USA). Data were analyzed for normal distribution with the Kolmogorov–Smirnov test and for homogeneity of variance with the Levene test. If variables met assumptions of normality and homogeneity of variance, an independent sample t test was used to compare the clinical data. Constituent ratio data were evaluated with chi-square (X²) tests. Binary logistic regression was performed to identify correlates of heavy bleeding. A two-tailed significance test was used for all comparisons and statistical significance was defined as P < 0.05.

Results

The main clinical data of patients with PCSP are shown in Table 1. The PCSP gestational age was 73.1 ± 21.7 days and the maximum mass diameter was 3.6 ± 1.6 cm.

All patients with PCSP presented with different degrees of vaginal bleeding: 14/38 (37%) patients complained of heavy vaginal bleeding and were treated by emergency intervention, while 21/38 (55%) patients suffered heavy bleeding (> 200 ml) before or during treatment. A maximum mass diameter of ≥ 3.5 cm and a gestational age of ≥ 70 days were risk factors for heavy bleeding (P < 0.05) (Tables 2 and 3). The presence of a rich vascular pattern in the area of the PCSP mass was detected by ultrasound in 33/38 (87%) patients.

Six patients with a PCSP gestational age of 64.2 ± 6.2 days and a mass diameter of 2.5 ± 0.6 cm were
successfully treated with medical treatment alone, while 32 patients with a PCSP gestational age of 74.8 ± 23.1 days and a mass diameter of 3.8 ± 1.6 cm were successfully treated with surgical or combined treatment. There was no significant difference between the two treatment groups in terms of the maximum diameter of the PCSP mass \((P < 0.05)\) (Table 4).

Three patients with PCSP (No. 1, 2 and 3) were treated with combined treatment. All had tried medical treatment, but were ultimately treated successfully with surgical treatment. The maximum diameter of the PCSP masses increased from 2.1 to 2.6 cm, 2.7 to 4.7 cm and 6.2 to 6.3 cm and serum \(\beta\)-hCG levels fell by 9 %, 19 % and 76 % between days 4 and 7 of the medical treatment in patients No. 1, 2 and 3, respectively. One patient (No.1) was eventually treated by hysteroscopy-guided surgical evacuation because the serum \(\beta\)-hCG level had not reduced and the PCSP mass continued to grow. Two patients (No. 2 and 3) were treated by laparoscopic and laparotomy resection of the lesion and uterine repair for heavy bleeding and PCSP mass growth, respectively.

Trophoblast infiltration into the myometrium was confirmed by pathology in eight patients who were treated by PCSP mass resection. Pathology confirmed the infiltration of trophoblasts into the bladder in one patient with a PCSP gestational age of 62 days, a mass diameter of 5.1 cm and a normalized serum \(\beta\)-hCG level \(< 5 \text{ IU/L}\), who was subsequently treated by resection of the PCSP mass and repair of the bladder.

None of the PCSP patients experienced major complications (such as hemodynamic instability, uterine scar rupture and hysterectomy).

### Discussion

Cesarean scar pregnancy is a dangerous form of ectopic pregnancy. PCSP is a rare and special type of CSP that is resistant to conservative treatment and is the major reason for secondary intervention.\(^{15}\) PCSP is a relatively newly recognized problem. PCSP incidence after surgical evacuation has been reported as 10/232 (4.35%)-7/116 (6%).\(^{13,14}\) A lack of vigilance and a limited understanding probably contributes to the underreported rate of PCSP.

### Table 1 Clinical characteristics of 38 patients with PCSP

| Characteristic                  | Result            |
|--------------------------------|-------------------|
| Age (years)                    | 32.3 ± 4.5        |
| Gravida (n)                    | 3.4 ± 1.9         |
| Prior cesarean delivery (n)    | 1 (1–3)           |
| Time from prior cesarean delivery (years) | 4.8 ± 3.5     |
| Residual myometrium thickness (cm) | 0.18 (0.1–0.5)  |
| Gestational age at diagnosis (days) | 73.1 ± 21.7   |
| Serum \(\beta\)-hCG level (IU/L) | 4264.4 (0.4–69615.0) |
| Maximum diameter of PCSP mass (cm) | 3.6 ± 1.6        |
| Interval between initial and terminal treatment (days) | 22.0 ± 12.7 |

Data are presented as mean ± standard deviation, medium (range), or number (%). \(\beta\)-hCG, \(\beta\)-human chorionic gonadotropin; PCSP, persistent cesarean scar pregnancy.

### Table 2 Comparison of basic and clinical characteristics of patients with and without heavy bleeding

| Characteristics                                      | Patients without heavy bleeding (n = 17) | Patients with heavy bleeding (n = 21) | \(P\)  |
|------------------------------------------------------|----------------------------------------|--------------------------------------|--------|
| Age (years)                                          | 31.8 ± 4.2                             | 32.6 ± 4.9                           | 0.596  |
| Prior cesarean delivery (n)                          | 1.4 ± 0.6                              | 1.2 ± 0.4                            | 0.214  |
| Interval since last caesarean delivery (years)       | 4.2 ± 3.6                              | 5.2 ± 3.4                            | 0.397  |
| Residual myometrium thickness (cm)                   | 0.22 ± 0.12                            | 0.20 ± 0.10                          | 0.743  |
| Gestational age at diagnosis (days)                  | 63.8 ± 18.5                            | 80.7 ± 21.5                          | 0.014* |
| Gestational age before termination \(>70\) days (N (\%)) | 3 (18\%)                              | 15 (71\%)                           | 0.001* |
| Serum \(\beta\)-HCG level (IU/L)                     | 15380.2 ± 20351.0                      | 5697.2 ± 78655.5                     | 0.079  |
| Maximum diameter of PCSP mass (cm)                   | 2.6 ± 0.8                              | 4.4 ± 1.6                            | 0.000* |
| Diameter of the gestational mass \(\geq 3.5\) cm (N (\%)) | 2 (12\%)                              | 15 (71\%)                           | 0.000* |
| Use of UAE, N (\%)                                   | 11 (64\%)                             | 17 (81\%)                           | 0.223  |
| Embryonic cardiac activity, N (\%)                   | 9 (56\%)                               | 8 (42\%)                            | 0.311  |
| Exogenous cesarean scar pregnancy, N (\%)            | 5 (29\%)                               | 7 (33\%)                            | 0.539  |
| Abundant blood flow of the mass, N (\%)              | 15 (88\%)                             | 18 (86\%)                           | 0.604  |

Data are presented as mean ± standard deviation or n (\%). \(\beta\)-hCG, \(\beta\)-human chorionic gonadotropin; PCSP, persistent cesarean scar pregnancies; UAE: Uterine artery embolization. * t test or \(X^2\) test.
Patients with PCSP are more prone to acute heavy vaginal bleeding than those with intact CSPs. Thus, PCSP can present as a more serious health risk than its original presentation as an intact CSP. The incidence of spontaneous heavy bleeding requiring emergent treatment of an intact CSP in the first trimester has been reported as 1/191 (0.5%)–2/78 (3%).13,18 All patients with PCSP in our study presented with different degrees of vaginal bleeding, with 14/38 (37%) complaining of heavy vaginal bleeding. A previous study reported that 11 patients with PCSP suffered heavy vaginal bleeding and two underwent hysterectomy to arrest the heavy bleeding.13,19 In our study, 21/38 (55%) patients with PCSP suffered heavy bleeding (>200 ml) before or during PCSP treatment. We determined that a maximum mass diameter of ≥3.5 cm and PCSP gestational age ≥70 days were risk factors for heavy bleeding, consistent with previous studies that reported a maximum mass diameter of ≥6 cm and gestational age ≥8 weeks as significant risk factors for heavy bleeding at CSP evacuation.20

The PCSP gestational age was 10.4 ± 3.1 weeks, which was advanced compared to the gestational age in patients (53 days, range, 29–129 or 7.5 ± 2.5 weeks).13,21 interval between initial treatment and PCSP diagnosis was 22.0 ± 12.7 days in our study. Other investigators have suggested that routine transvaginal ultrasound should be performed to detect pregnancy remnants two weeks after surgical evacuation.12,14 If an ultrasound revealed pregnancy remnants, hysteroscopy was performed to identify the position of the remaining tissue, which was then removed by surgical evacuation.12 This is good method to ensure early diagnosis and management of PCSP.

A CSP mass mainly consists of the embryo sac, while a PCSP mass consists of residual gestational tissue and substantial hemorrhagic necrotic tissue.15 As such, PCSP masses have certain specific imaging features. Multiple echogenic patterns can be detected within a PCSP or heterogeneous mass by ultrasound.22 The maximum diameter of a PCSP mass in our study was 3.6 ± 1.6 cm, similar to previous findings of a median mean diameter of 3.6 cm (range 1.5–5.8).13 The size of the PCSP mass was larger than the intact gestational sac, which was 1.73 cm in diameter (range 0.3–7.4).13 The presence of a rich vascular pattern in the area of the cesarean scar is imperative to diagnose CSP by ultrasound, but is not imperative for a diagnosis of PCSP. In our study, a rich vascular pattern in the area of the PCSP mass was found in 33/38 (87%) patients.

Several factors are associated with the formation of a PCSP mass. Firstly, a prior study confirmed that a previous cesarean scar defect is a common presentation among women with CSP23,24 and trophoblastic tissue is

### Table 3 Logistic regression of significant variables

| Variable                                      | B   | Wald† | P*  | OR (95% CI)     |
|-----------------------------------------------|-----|-------|-----|-----------------|
| Maximum diameter of PCSP mass (≥3.5 cm)       | 2.58| 7.17  | 0.007| 13.18 (2.00–87.10) |
| Gestational age at diagnosis (≥70 days)       | 2.05| 5.03  | 0.025| 7.726 (1.29–46.17) |

*P value for specific categories refers to significant difference present among the categories. †Wald test for entire group. CI, confidence interval; OR, odds ratio; PCSP, persistent cesarean scar pregnancy.

### Table 4 Comparison of clinical characteristics of patients successfully treated with medical treatment only versus those successfully treated with surgical or combined treatment

| Characteristic                                      | Medical treatment only (n = 6) | Surgical or combined treatment (n = 32) | P    |
|-----------------------------------------------------|-------------------------------|----------------------------------------|------|
| Maximum CSP mass diameter before termination (cm)   | 2.5 ± 0.6                     | 3.8 ± 1.6                              | 0.072|
| ≥3.5 cm                                             | 0 (0%)                        | 17 (53%)                               | 0.016*|
| <3.5 cm                                             | 6 (100%)                      | 15 (47%)                               |      |
| Gestational age before termination (days)           | 64.2 ± 6.2                    | 74.8 ± 23.1                            | 0.276|
| ≥70 days                                            | 1 (17%)                       | 17 (53%)                               | 0.101|
| <70 days                                            | 5 (83%)                       | 15 (47%)                               |      |
| Serum β-hCG level before termination (IU/L)        | 71601.1 ± 437678.7            | 45813.9 ± 35039.6                      | 0.120|

Data are presented as mean ± standard deviation or n (%). β-hCG, β-human chorionic gonadotropin; CSP, cesarean scar pregnancy. *: X2 test
located within the defect, making it inaccessible for surgical evacuation. Thus, the proportion of women who underwent surgical evacuation of CSP diagnosed with retained product of contraception on postprocedure ultrasound examination was higher when compared to women who underwent surgical evacuation of failed intrauterine pregnancies. Secondly, a CSP mass can penetrate into the myometrium through a microdehiscence tract or through a conspicuous defect over the previous uterine cesarean section scar. Infiltration of trophoblasts into the myometrium or even the bladder was confirmed in our study. In these cases, resection of the PCSP mass or hysterectomy is the most efficient method to remove all of the trophoblast cells. Thirdly, incomplete removal of the embryo sac will cause local hemorrhage and the surrounding scar tissue hinders absorbance. These factors all contribute to the persistent remains of an ectopic pregnancy mass.

Treatment for PCSP is challenging. The treatment plan needs to be individualized. Surgery is the main treatment for PCSP. Only a few reports have described PCSP treatment and such cases were mainly treated by surgical or combined treatment. A diagnosis of PCSP is either presented directly by previous study or conferred from the description of the disease. Zhang et al. reported that eight patients with PCSP were treated successfully by laparoscopic scar pregnancy resection and scar-defect repair, while two patients were treated by hysteroscopy. In Li et al.’s study, six patients with PCSP were treated by repeat surgical evacuation with hysteroscopy guidance. In their study, Wu et al. reported that 10 patients with PCSP were treated by hysteroscopy followed by MTX. Jurkovic et al. reported that seven patients with PCSP were treated with ultrasound-guided repeat surgical evacuation. In Polat et al.’s study of three patients with PCSP, one was treated by an emergent wedge excision of the PCSP mass, the second was treated by an emergent hysterectomy and the third patient was treated by a systemic single intramuscular dose of MTX (50 mg/m2). In our study, 32/38 (84%) patients were managed by surgical treatment: 24 by repeat surgical evacuation and eight by PCSP mass resection. Surgical evacuation is the most effective method for treating PCSP. Similar to exogenous CSP, resection of an exogenous PCSP mass has been efficient in our experience, especially in cases of trophoblast infiltration into the bladder.

Although a previous study suggested that medical treatment may not be optimal for the treatment of PCSP, medical treatment of PCSP has become an attractive alternative in our experience, especially for hemodynamically stable patients with a maximum mass diameter of < 3.5 cm. Systemic MTX therapy is an effective and safe treatment for CSP, especially in cases of early diagnosis. Systemic MTX for CSP is used in hemodynamically stable patients, with a gestation age of < 8 weeks, serum hCG level < 5000 IU/L and gestational sac ≤ 2.5 cm. For limited cases, we found that a maximum PCSP mass diameter of < 3.5 cm is the main indication for medical treatment, which is different to the indications for medical treatment of CSP. Our study found that gestational age was younger in the medical treatment only than in the surgical or combined treatment group, and there was a significant difference between these groups. The mean serum β-hCG level was higher in the medical treatment only group as a result of several patients with low serum β-hCG levels and large PCSP masses treated with surgical treatment. These results indicate patients with PCSP show particular clinical characteristics that cannot be treated using CSP treatment methods.

Our study was limited by a small sample size and a lack of multicenter data. The indications for different treatments for PCSP could not be definitely identified. A randomized, controlled study with a larger patient sample is needed in future to make up for these deficiencies.

Conclusion

In conclusion, PCSPs are diagnosed at advanced gestational age and patients are more prone to heavy bleeding. Surgery is the main and most effective treatment for PCSP. Medical treatment of PCSP has become an attractive alternative, especially for patients with a maximum PCSP mass diameter of < 3.5 cm.

Disclosure

The authors declare that they have no conflicts of interest.

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