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Original Research

Clinical analysis of 211 cases of cesarean scar pregnancy

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Summary

Objective: To investigate the rational choice of early diagnosis and treatment of cesarean scar pregnancy (CSP). *M ethods:* The clinical data, including age, gravidity, time to previous cesarean section, first symptom, auxiliary examination, regimen, and therapeutic outcomes, of 211 patients with CSP admitted to Sichuan Provincial People's Hospital from March 2016 to February 2018 were retrospectively analyzed. *Results:* Of the 211 patients, 165 patients were first diagnosed with CSP in this hospital, and eight of them (4.85%) were misdiagnosed; 46 patients were referred to thus hospital by physicians in other hospitals, and 21 of them (45.65%) were misdiagnosed. After admission, transvaginal color Doppler sonography was performed with a blood β-human chorionic gonadotropin (β-hCG) study to confirm the diagnosis. According to the surgical approaches, 211 patients were divided into six groups: group A: hysteroscopy group (141 patients), group B: uterine artery embolization (UAE) plus hysteroscopy group (38 patients), group C: hysteroscopy plus laparoscopy group (seven patients), group D: UAE with hysteroscopy plus laparoscopy group (six patients), group E: laparotomy group (12 patients), and group F: uterine evacuation group (seven patients). There were no significant differences in age, number of cesarean sections, time from previous cesarean section, days of the missed period, diameter of the gestational sac, or blood β-hCG levels among the six groups ($p > 0.05$). However, the cure rate, complication rate, mean intraoperative blood loss, mean operative time, mean length of hospital stay, and mean medical cost were all statistically significant between the six groups ($p < 0.05$). *Conclusions:* Women who have a history of cesarean section should be vigilant and undergo a transvaginal ultrasound examination as early as possible to exclude CSP and avoid a missed diagnosis or misdiagnosis. For patients at less than or equal to eight weeks of gestation and with a gestational sac diameter less than or equal to 3.0 cm, hysteroscopy is the preferred treatment that is safe and effective. Hysteroscopy combined with laparoscopy and laparotomy are suitable for patients with a high risk of massive bleeding, for instance, patients with a thin anterior myometrium on which abundant blood flow signals are shown, or should be considered as emergency backup plans for other surgical approaches. UAE can effectively reduce intraoperative blood loss but increases the risk of postoperative complications, length of hospital stay, medical costs, and it is suitable for patients with massive bleeding during or after CSP surgery and in need of emergency hemostasis or for patients with a very high risk of bleeding confirmed by a preoperative assessment.

Key words: Cesarean scar pregnancy; Hysteroscopy; Uterine artery embolization; Laparoscopy.

Introduction

Cesarean scar pregnancy (CSP) refers to a special type of ectopic pregnancy where the embryo is implanted at the scar site from the previous cesarean section. Delayed diagnosis and treatment may cause serious complications including a ruptured uterus, massive bleeding, and even excision of the uterus, which leads to the loss of fertility in patients. More clinical attention should be paid to CSP. In this study, 211 patients with CSP who were admitted to this hospital from March 2016 to February 2018 were selected to investigate the reasonable choice of early diagnosis and treatment of CSP.

Material and Methods

A total of 211 patients with CSP who were admitted to the Department of Obstetrics and Gynecology of Sichuan Provincial People's Hospital from March 2016 to February 2018 were selected as the study subjects. The clinical data of the patients were collected, including age, gravidity, time to last cesarean section, first symptom, auxiliary examinations, treatment regimens, and treatment outcomes. The mean age, gravidity, number of cesarean sections, and time to the last cesarean section of the 211 patients was 32.51 ± 4.87 (range: 20-46) years, 3.28 ± 0.65 (range: 2-11) times, 1.24 ± 0.33 (range: 1-3) times, and 4.16 ± 2.56 (range: 0.7-19) years, respectively. Of the 211 patients, 165 patients were first diagnosed with CSP in this hospital, and eight of them (4.85%) were misdiagnosed as an incomplete abortion or cervical pregnancy; 46 patients were referred to this hospital by physicians in other hospitals, and 21 of them (45.65%) were misdiagnosed. Among the referred patients, 13 patients had undergone an induced abortion or excavation of the uterus, including three patients with intraoperative bleeding and ten patients with incomplete evacuation of the uterus. After admission, transvaginal color Doppler sonography was performed with a blood β-human chorionic gonadotropin (β-hCG) study to confirm the diagnosis; if necessary, contrast-enhanced ultrasonography or MRI was used to make the diagnosis.

The patients could not be randomly grouped due to factors including medical safety, physician's experience, and fertility preservation. Therefore, they were divided according to the patient's preference of surgical approach. According to the surgical approaches, 211 patients were divided into six groups: group A: hysteroscopy group (141 patients), group B: uterine artery em-

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bolization (UAE) plus hysteroscopy group (38 patients), group C: hysteroscopy plus laparoscopy group (seven patients), group D: UAE with hysteroscopy plus laparoscopy group (six patients), group E: laparotomy group (12 patients), and group F: uterine evacuation group (seven patients).

Plasma bipolar hysteroscopy system was used in this study. The intrauterine pressure was generally maintained at 100-120 mmHg after uterine distention using a distending medium (5% glucose or normal saline). After routine disinfection, the cervix was dilated with an F10 dilator. The hysteroscope was placed to explore the position and size of the gestational sac. The suction tube (F7 or F8) was used to quickly aspirate the gestational tissue, as repeat evacuation and curettage should be avoided at the site of the cesarean scar. Oxytocin (10 u) was injected onto the uterine wall or administered intravenously to promote uterine contractions. Then, the hystero- scope-guided loop electrosurgical excision procedure was used to remove residual gestational tissue and electrocoagulate active bleeders.

The femoral artery region was routinely disinfected and draped. Under local anesthesia, a femoral artery puncture was performed using the Seldinger technique. After a successful puncture, a 5F-RUS catheter was placed for bilateral uterine artery angiography. After methotrexate (MTX, 25 mg) was injected, embolization with gelatin sponge particles was performed in the bilateral uterine arteries. Further surgical treatment was typically performed within 48-72 hours after UAE.

Pneumoperitoneum of CO_2 was established under general anesthesia. The peritoneal reflection of the urinary bladder was incised to press the bladder downward. The hysteroscope was used to explore the position and size of the gestational sac. Under laparoscopic guidance, the suction tube (F7 or F8) was used to remove most of the gestational tissue, and the residual gestational tissue and decidua were then cleared. Continuous suturing of the myometrium and serosal layer was performed with a 2-0 barbed suture, and the abdomen was closed routinely.

The abdominal cavity was accessed following a routine procedure. The peritoneal reflection of the urinary bladder was incised to press the bladder downward. The myometrium of the uterus was transversely incised at the most prominent part of the cesarean scar to remove the gestational tissue. After confirmation of no residual gestational tissue or decidua in the uterus, a 2-0 absorbable suture was used to close the myometrium and serosal layer in double rows. The abdomen was closed as routine.

All evacuation procedures were performed under ultrasound guidance. After routinely disinfecting and draping the patient, the cervix was dilated with a dilator (F7.5-8.5). An F7 or F8 suction tube was used to aspirate the gestational tissue around the uterine cavity 2-3 times. Then, a curette was used to gently explore the presence of residual gestational tissue in the uterine cavity and lower portion of the uterus. Repeat evacuation and curettage should be avoided at the site of cesarean scar.

Intraoperative blood loss, operative time, days of hospitalization, and medical costs were documented. The cure criteria were defined as follows: follow-up color Doppler ultrasound showed no residual gestational tissue in the uterine cavity within one month after surgery, and the blood β-hCG decreased to a normal level.

The SPSS 16.0 software package was used for the statistical analysis. Quantitative data with homogeneity of variances were compared using a *t*-test. Data with inhomogeneity of variances were also compared using a *t*-test. A X^2 test was used to compare the counted data.

Results

There were no significant differences in age, number of cesarean sections, time from previous cesarean section, days of the missed period, diameter of the gestational sac, or blood β-hCG levels among the six groups ($p > 0.05$) (Table 1).

Differences in the cure rate, complication rate, mean intraoperative blood loss, mean operative time, average length of hospital stay, and average medical cost were all statistically significant among the six groups ($p < 0.05$) (Table 2). The cure rate of group F was significantly different from that of the other groups ($p < 0.05$). In group F, one patient had massive intraoperative blood loss of approximately 800 ml; another patient had residual gestational tissue and underwent a secondary hysteroscopic surgery. The complication rates in groups B, D, and F were statistically significant compared with the other groups ($p < 0.05$). In group A, two complications were reported: one patient had a massive intraoperative blood loss of approximately 1,200 ml, and another patient had a perforated uterus that was repaired via hysteroscopic and laparoscopic surgery. In group B, two cases of deep vein thrombosis (DVT) after UAE, three cases of hypomenorrhea or amenorrhea, and one case of premature ovarian failure were reported. In group D, one case of DVT after embolization was reported. The mean intraoperative blood loss in groups E and F was significantly different from that in the other groups ($p < 0.05$). The mean operative times in groups A, E, and F were significantly different from that in the other groups ($p < 0.05$), of which the mean operative time was shorter in groups A and F but was longer in group E. The average length of the hospital stay in groups A and F was significantly different from that in the other groups ($p < 0.05$), and both were shorter than that in the other groups. The average medical cost of patients in each group was statistically significant ($p < 0.05$). The average medical cost was ranked from lowest to highest as follows: groups A and F, groups C and E, and groups B and D. The uterus was preserved in all patients.

Discussion

To date, the incidence of CSP is approximately 1:1,800 to 1:2,216, accounting for 1.15% of pregnancies in women with a history of cesarean section and 6.10% [1] of ectopic pregnancies in women with a history of cesarean section. The cesarean section rate is approximately 35% in China, which is far higher than the alert line of 15% defined by the World Health Organization (WHO). The incidence of CSP has demonstrated an upward trend. The early manifestation of CSP includes a small amount of vaginal bleeding, dull abdominal pain, and other non-specific clinical manifestations of early pregnancy. Of the 211 patients, 165 patients were first diagnosed with CSP in this hospital, and

Table 1. — *Comparison of general data between groups (c±S)*

	Group A	Group B	Group C	Group D	Group E	Group F
Number of patients	141	38	7	6	12	7
Age (years)	32.11±3.26	31.78±2.57	32.91±3.14	32.25±1.79	31.39±2.77	33.01±2.55
Number of cesarean sections	1.19±0.61	1.37±0.38	1.14±0.24	1.43±0.51	1.25±0.24	1.00±0.00
Time from previous cesarean section (years)	4.67±2.68	4.33±2.71	5.03±1.96	4.61±2.36	3.87±1.55	3.96±2.44
Days of the missed period	50.89±7.65	55.04±10.76	52.77±8.41	57.33±4.66	56.33±6.11	48.07±5.26
Gestational sac diameter (cm)	2.75±2.12	3.16±1.56	3.07±2.13	3.20±0.98	3.01±1.55	2.61±0.51
Blood β-hCG levels (mIU/ml)	24050.66± 15607.65	28654.17± 12644.31	26631.12± 9566.33	30156.98± 14655.11	26917.23± 10599.34	22966.41± 17734.19

Table 2. — *Comparison of the therapeutic effectiveness in each group (`c±S)*

	Group A	Group B	Group C	Group D	Group E	Group F
Cure rate (%)	98.58	100.00	100.00	100.00	100.00	85.71
Complication rate (%)	2.84	15.79	0.00	16.67	0.00	28.57
Average intraoperative blood loss (ml)	48.13±7.99	65.22±8.01	49.33±6.98	50.21±5.00	107.52±9.31	114.11±4.62
Average operative time (min)	26.50±6.33	49.00±11.22	52.21±4.13	50.45±5.52	70.60±9.30	17.71±9.47
Average length of hospital stay (days)	4.26±0.55	6.29±1.39	7.67±2.44	9.02±2.68	7.83±1.19	4.21±3.11
Average medical cost (yuan)	5905.24± 855.30	21014.88± 2566.77	12008.00± 1126.33	30096.58± 2855.71	10860.17± 957.13	4001.20± 266.37

eight of them (4.85%) were misdiagnosed; 46 patients were referred to our hospital by physicians in other hospitals, and 21 of them (45.65%) were misdiagnosed. Misdiagnosis or a missed diagnosis often leads to blind evacuation of the uterus, drug-induced abortion, or delayed termination of the pregnancy, which may cause massive bleeding, infection, and even excision of the uterus. Loss of fertility is a severe consequence of excision of the uterus. With this respect, early diagnosis is very important [2]. The present authors emphasize that early ultrasonography should be performed in women with a history of cesarean section as soon as possible to rule out CSP. A transvaginal color Doppler sonography examination is the first-line choice. If the ultrasound cannot clearly show the relationship between the gestational sac and the uterine wall, bladder, or other surrounding organs, an enhanced ultrasound or MRI could be selected for a diagnosis. Blood β-hCG levels are not specific for the diagnosis of CSP but are of great significance during follow-up to evaluate the therapeutic effects after surgery. In addition, the abnormal increase of blood β-hCG levels may be an alerting sign indicating the possibility of a gestational trophoblastic tumor.

Due to the lack of large randomized controlled studies, there are no unified guidelines for the diagnosis and treatment of CSP in or outside of China. The main treatments include local/systemic drug therapy, evacuation of the uterus, hysteroscopy, hysteroscopic and laparoscopic surgery/laparotomy, and hysteroscopic and laparoscopic surgery after UAE. Conservative medication alone is no longer used in this hospital due to the uncertain effectiveness, long treatment cycle, high failure rate, and risk of massive bleeding. In contrast, surgical treatment is more proactive and can avoid further progression of the condition and other serious consequences such as massive bleeding and hysterectomy. Evacuation of the uterus is a simple, economical, and quick-to-recover procedure, but has a high risk of fatal massive bleeding. Once incomplete evacuation has occurred, repeat evacuation of the uterus might be required and can increase patient suffering. In this study, the evacuation group included seven patients. One patient suffered massive bleeding during the evacuation procedure. The intraoperative blood loss was approximately 800 ml. The bleeding amount decreased after uterine compression using an intrauterine balloon. Another patient had residual gestational tissue and underwent a secondary hysteroscopic surgery. The cure rate of the evacuation group was 85.71%, and the complication rate was 28.57%. Therefore, evacuation of the uterus should not be used as the first choice for CSP treatment. The surgical resection of lesions is one of the safe and effective treatments for CSP. The procedure includes laparoscopic surgery and laparotomy, and it can completely remove lesions and repair scars. However, this procedure may be associated with large trauma, a longer operative time, longer recovery time, higher medical cost, and lower treatment acceptance rate. Moreover, laparoscopic surgery requires qualified surgeons and an appropriate facility and equipment. Laparotomy should be selected in patients with a high degree of suspicion of uterine rupture, sign of uterine rupture, difficulty with intraoperative hemostasis, or unpredictable organ or blood vessel damage. Laparotomy has less strict requirements on surgical skills and equipment and can ensure thorough removal of the lesions and repair of the scar site; therefore, it is suitable for hospitals at all levels and considered an emergency rescue procedure. In this study, the regimens in groups C and E successfully removed the lesions and achieved a cure rate of 100% and preserved the fertility of the patients, and no serious complications were reported during or after surgery,

but the regimens were associated with higher medical costs, a longer operative time, and longer hospital stay. Therefore, hysteroscopic and laparoscopic surgeries and laparotomy are only suitable for patients with a high risk of massive bleeding, for instance, patients with a thin myometrium on which abundant blood flow signals are shown, or should be considered as emergency plans for other surgical treatments.

Since Wang *et al.* first reported the hysteroscopic removal of CSP lesions in 2005, the unique advantages of hysteroscopy for CSP treatment have drawn our attention [3]. The size of the gestational sac, the site of implantation, and the distribution of blood vessels can be observed under direct vision. Hysteroscopy can completely remove the lesions, avoiding secondary surgery, and shorten the follow-up period. Hysteroscopy can reduce the incidence of uterine perforation. Hemostasis by coagulation is reliable and can reduce intraoperative blood loss. Hysteroscopy can observe the shape of the uterine cavity and endometrial thickness. There is a short operative time, no concerns for the wound scar, rapid recovery, higher treatment acceptance rate, and preservation of fertility [3]. However, the safety of the removal of CSP lesions in patients with a large amount of vaginal bleeding, large gestational sacs, or protruding CSP lesions in the anterior wall of the uterus has not been confirmed. In this study, group A included 141 patients, with a cure rate of 98.58% and a complication rate of 2.84%. Two patients had complications. In a patient who missed her period for 8+4 weeks, the size of the gestational sac was approximately 4.0×3.5 cm, and her preoperative blood β-hCG level was 25,037.00 mIU/ml. She suffered a massive intraoperative blood loss of 1,200 ml, and the bleeding was controlled after intraoperative emergency UAE. In another patient who missed her period for 7+2 weeks, the size of the gestational sac was approximately 3.0×2.6 cm, and her preoperative blood β-hCG level was 18,910.00 mIU/ml. Uterine perforation occurred during hysteroscopy, and laparo- scopy was immediately performed to remove the CSP lesion and repair the perforation site. Overall, group A had a higher cure rate, lower complications rate, less intraoperative blood loss, shorter average operative time, shorter length of hospital stay, and lower medical cost. Thus, hysteroscopy was the preferred treatment for most patients with CSP. However, for patients with a missed period longer than eight weeks and gestational sac size larger than 3 cm, or a large amount of vaginal bleeding before surgery, surgeons should be highly vigilant about the risk of massive bleeding. To ensure clinical safety, adequate preoperative assessment of transfusion, preparation of laparoscopic or laparotomy equipment, and readiness of the medical team should be ensured, and preparation for an emergency UAE should be considered in case of emergency.

UAE is a new technique combined with arterial embolization and arterial infusion chemotherapy. After a bilateral uterine arterial infusion of MTX, gelatin sponge particles are used to embolize the arteries. UAE makes MTX locally highly concentrated and directly acts on intra-villous blood vessels to reduce the uterine blood supply and suppress embryo viability. Thus, UAE can reduce the risk of bleeding and improve surgical safety. Usually, further surgical treatment can start within 48-72 hours after UAE [4]. In recent years, UAE has been a well-accepted technique, with minimal damage and high safety, which best ensures the safety of life of patients with CSP and provides the opportunity to preserve the uterus. MTX is safe and effective; it does not increase the rate of miscarriage or malformation in subsequent pregnancies and has no adverse effects on the intelligence or physical ability of a newborn. Moreover, gelatin sponge particles can be resorbed. In most patients, blood vessels can be recanalized within 10-20 days. Therefore, UAE has been widely used [5]. However, a series of complications during and after UAE cannot be ignored, including hematoma in the puncture site, arterial rupture, venous thrombosis of the legs, premature ovarian failure, and amenorrhea. In this study, there were two cases of DVT in the legs, three cases of hypomenorrhea or amenorrhea, and one case of premature ovarian failure after surgery in group B. The complication rate was 15.79%. There was one case of DVT in the leg in group D. The complication rate was 16.67%. The three patients with DVT underwent successful thrombectomy. The complication rates in groups B and D were statistically significant compared with other groups ($p < 0.05$). The mean length of hospital stay and average medical costs in groups B and D were significantly higher than those in the other groups ($p < 0.05$). Therefore, UAE should not be used as a routine preoperative treatment for patients with CSP. UAE is only applicable to emergency hemostasis when massive bleeding occurs during or after surgery for CSP, or to be used in patients with a high risk of massive bleeding at the preoperative assessment.

Conclusion

In summary, CSP has emerged in this era, and its incidence is unclear due to a lack of statistical data from a large sample size. It is recommended that vaginal ultrasound be performed as early as possible in women with a history of cesarean section if pregnant again. Once CSP is diagnosed, the pregnancy should be terminated as soon as possible. For patients with a missed period no longer than eight weeks and gestational sac diameter no larger than 3.0 cm, hysteroscopic surgery is a safe, effective, and preferred treatment. Hysteroscopic and laparoscopic surgery and laparotomy are only suitable for patients with a high risk of massive bleeding, for instance, patients with a thin myometrium that has abundant blood flow signals, or should be considered as emergency plans for other surgical treatments. UAE can effectively reduce the amount of intraoperative blood loss, but increases the risk of postoperative complications, length of hospital stay, and medical cost. UAE is only applicable to emergency hemosta-

sis when massive bleeding occurs during or after surgery for CSP, or to be used in patients with a high risk of massive bleeding at the preoperative assessment.

References

[1] Seow K.M., Huang L.W., Lin Y.H., Lin M.Y., Tsai Y.L., Hwang J.L.: "Cesarean scar pregnancy: issues in management". *Ultrasound Obstet. Gynecol.*, 2004, *23*, 247

[2] Family Planning Subgroup, Chinese Society of Obstetrics and Gynocology, Chinese Medical Association: "Expert opinion of diagnosis and treatment of cesarean scar pregnancy (2016)". *Zhonghua Fu Chan Ke Za Zhi*, 2016, *51*, 568. [In Chinese]

[3] Wang C. J., Yuen L. T., Chao A. S., Lee C. L., Yen C. F., Soong Y. K.:" Caesarean scar pregnancy successfully treated by operative hysteroscopy and suction curettage". BJOG, 2005, *112*, 839.

[4] Kutuk M.S., Uysal G., Dolanbay M., Ozgun M. T.: "Successful medical treatment of cesarean scar ectopic pregnancies with systemic multidose methotrexate: single□center experience". *J. Obstet. Gynaecol. Res.*, 2014, *40*, 1700.

[5] Lan W., Hu D., Li Z., Wang L., Yang W., Hu S.: "Bilateral uterine artery chemoembolization combined with dilation and curettage for treatment of cesarean scar pregnancy: a method for preserving the uterus". *J. Obstet. Gynaecol. Res.,* 2013, *39*, 1153.

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