Analysis of Clinical Characteristics, Diagnosis, and Treatment of Different Types of Cesarean Scar Pregnancy (Postprint)

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Abstract

Background: Current classification of cesarean scar pregnancy (CSP) is based solely on ultrasonographic features, and there is currently a lack of analysis and summary of clinical characteristics of different CSP types under this classification standard. Objective: To investigate the clinical features and differences in diagnosis and treatment among different types of CSP. Methods: A total of 862 CSP patients admitted to the Department of Obstetrics and Gynecology, Peking University Third Hospital from July 2014 to June 2022 were included as study subjects. According to ultrasound classification criteria, they were divided into Type I, Type II, and Type III groups, and their clinical characteristics and diagnosis/treatment indicators were retrospectively analyzed. Results: In this study, Type I group accounted for 36.5% (315/862), Type II group for 53.1% (458/862), and Type III group for 10.3% (89/862) of CSP patients. The incidence of abdominal pain was 24.2% (209/862) and vaginal bleeding was 65.0% (560/862) among CSP patients. There were no statistically significant differences in the incidence of abdominal pain and vaginal bleeding among the three groups (P=0.261, P=0.062). Patients in Type III group had gestational age at diagnosis of 55 (46, 64) days, mean gestational sac diameter of 29.6 (19.1, 43.3) mm, preoperative serum β-human chorionic gonadotropin (β-HCG) level of 60,673 (17,164, 122,203) mU/mL, rates of requiring ancillary embryocidal drug therapy, surgery under laparoscopic monitoring, and uterine artery occlusion of 27% (24/89), 33.7% (30/89), and 32.6% (29/89) respectively, operation duration of 101 (67, 125) minutes, hospital stay of 4 (3, 7) days, treatment cost of 11,933.7 (8,760.7, 15,250.6) yuan, postoperative 24-hour cumulative blood loss, incidence of bleeding $ $200 mL, and blood transfusion rate of 83 (33, 178) mL, 24.7% (22/89), and 7.9% (7/89) respectively, all higher than the other two groups (all P<0.001). The overall incidence of persistent CSP was 3.1% (27/862), with no statistically significant difference among the three groups (2 =3.353, P=0.187). Conclusion: There were no significant differences in clinical

characteristics such as age, obstetric history, previous uterine surgical history, abdominal pain, and vaginal bleeding among different types of CSP patients. Type I and II patients had less invasive treatments, while Type III patients consumed more medical resources and required multidisciplinary team and individualized management. With standardized management, treatment outcomes were satisfactory for all types.

Full Text

Clinical Characteristics and Management of Different Types of Cesarean Scar Pregnancy

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Abstract

Background: The current classification of cesarean scar pregnancy (CSP) is based solely on ultrasonic characteristics. At present, there is a lack of analysis and summarization of the clinical characteristics of different types of CSP cases under this classification system. **Objective:** To investigate the clinical characteristics and management differences among different types of CSP. **Methods:** A total of 862 CSP patients admitted to the Department of Obstetrics and Gynecology at Peking University Third Hospital from July 2014 to June 2022 were enrolled and divided into type I, type II, and type III groups according to ultrasound classification criteria. Clinical characteristics and treatment indicators were retrospectively analyzed. **Results:** Among all CSP patients, 36.5% (315/862) were type I, 53.1% (458/862) were type II, and 10.3% (89/862) were type III. The incidence of abdominal pain was 24.2% (209/862) and vaginal bleeding was 65.0% (560/862) in CSP patients. There was no significant difference in abdominal pain (P=0.261) or vaginal bleeding (P=0.062) among the three groups. In type III patients, the median gestational age at diagnosis was 55 (46, 64) days, the median diameter of the gestational mass was 29.6 (19.1, 43.3) mm, and the median serum β-HCG level was 60,673 (17,164, 122,203) mU/mL. The proportions requiring

adjuvant pharmacologic embryocidal therapy, laparoscopic monitoring during surgery, and uterine artery occlusion were 27% (24/89), 33.7% (30/89), and 32.6% (29/89), respectively. The median operation duration was 101 (67, 125) min, median hospitalization duration was 4 (3, 7) days, and median treatment cost was ¥11,933.7 (¥8,760.7, ¥15,250.6). The median accumulated bleeding volume within 24 hours after surgery, incidence of bleeding $ 200mL, andbloodtransfusionratewere83(33, 178)mL, 24.7^{2}$=3.353, P=0.187). **Conclusion:** There were no significant differences in age, maternal history, or clinical characteristics such as abdominal pain and vaginal bleeding among patients with different types of CSP. The treatment of type I and type II patients was less invasive and consumed fewer medical resources, while type III patients consumed more medical resources and had higher requirements for multidisciplinary team management and individualized care. The prognosis of all three types of patients was ideal after standardized management.

Keywords: Cesarean section; Scar pregnancy; Signs and symptoms; Treatment; Prognosis

Introduction

Cesarean scar pregnancy (CSP) is a serious complication in women with a history of cesarean section [1]. Due to its high risk of massive hemorrhage, uterine rupture, impaired fertility, or even loss of fertility, and significant heterogeneity in disease severity, CSP has attracted increasing attention from obstetricians and gynecologists in recent years [2-3]. Previous studies have reported risk factors for CSP, imaging diagnosis, and clinical application of related surgical procedures, but there remains a lack of summary analysis regarding the clinical characteristics of different types of patients under the current classification system.

The classification of CSP is a particularly important issue in clinical practice, involving multiple aspects such as patient selection of different levels of medical institutions, whether inter-institutional referral is required after diagnosis, and what medical resources institutions should possess. The 2016 Chinese Expert Consensus on the Diagnosis and Treatment of Cesarean Scar Pregnancy [4] (hereinafter referred to as the "2016 CSP Chinese Expert Consensus") first proposed a classification system dividing CSP into three types based on ultrasound imaging characteristics. This classification has been widely adopted in current clinical practice, but there has been no analysis or summary of the clinical characteristics of different types of CSP under this classification standard.

This study, based on a large sample of cases from the National Clinical Research Center for Obstetrics and Gynecology Diseases and Beijing Critical Maternal Referral Center, compares and analyzes patients' medical history, disease manifestations, laboratory data, and treatment courses to explore the clinical characteristics and treatment experience of different types of CSP patients, and

to compare the medical resource requirements and treatment outcomes among different types.

Methods

1.1 Study Subjects A total of 862 CSP patients admitted to the Department of Obstetrics and Gynecology at Peking University Third Hospital from July 2014 to June 2022 were enrolled as study subjects. **Inclusion criteria:** complete medical history and early pregnancy imaging data. **Exclusion criteria:** intrauterine pregnancy combined with cesarean scar pregnancy; conservative medical treatment alone; expectant management or continuation of pregnancy; patients who did not receive treatment at our hospital. Disease diagnosis was based on previously reported criteria [4].

1.2 Methods This study was a case-control study. According to the classification criteria of the 2016 CSP Chinese Expert Consensus [4], patients were divided into three groups: type I accounted for 36.5% (315/862), type II accounted for 53.1% (458/862), and type III accounted for 10.3% (89/862). Patient data were retrieved from the electronic medical record system to compare the clinical characteristics of different types of CSP patients. This study was approved by the Reproductive Medicine Ethics Committee of Peking University Third Hospital (2019SZ-069), and informed consent was waived.

1.3 Statistical Analysis SPSS 22.0 software was used for statistical analysis. Normally distributed measurement data were expressed as ($\bar{x}\pm s$) and compared using analysis of variance (if variance was homogeneous). Non-normally distributed measurement data were expressed as M (P_{25}, P_{75}) and compared using the Kruskal-Wallis rank sum test. According to clinical practice and previous studies from our center [10-11], some measurement data were converted to categorical data. Categorical data were described using relative numbers and compared using the ^{2} test; if differences among groups were statistically significant, pairwise comparisons were further performed using the Bonferroni method. $P<0.05$ (two-tailed) was considered statistically significant.

Results

2.1 General Clinical Data The mean age of the 862 CSP patients was $(34.6\$\pm4.6)years, with50.0$ \$35 years). The median gravidity was 3 (3, 5) and median parity was 1 (1, 2). The proportion of patients with $ \$2 previous cesarean sections was 33.5% (289/862), those whose first cesarean was performed before term accounted for 4.2% (36/862), and those who were not in labor at the time of first cesarean accounted for 89.3% (770/862). The proportion of patients who conceived through in vitro fertilization-embryo transfer (IVF-ET) in the

current pregnancy was 3.9% (34/862). There were no statistically significant differences in the above general clinical data among the three groups (P>0.05) .

The median interval between the current pregnancy and the last cesarean section (referred to as "pregnancy interval") was 5.25 (3.0, 8.5) years. A history of previous CSP was present in 4.9% (42/862) of patients, and 77.0% (664/862) had a history of previous uterine cavity surgery. There were no statistically significant differences among the three groups in pregnancy interval, previous CSP history, or uterine cavity surgery history (P>0.05) .

2.2 Diagnosis and Treatment Process The incidence of abdominal pain was 24.2% (209/862) and vaginal bleeding was 65.0% (560/862) in CSP patients. There were no statistically significant differences in the incidence of abdominal pain or vaginal bleeding among the three types of CSP patients (P=0.261, P=0.062). The median gestational age at diagnosis was 47 (42, 56) days, the median gestational mass diameter measured by ultrasound was 19.0 (12.3, 26.7) mm, the median preoperative serum β-HCG level was 41,510 (15,175, 94,888) mU/mL, and fetal cardiac activity was detected by ultrasound in 40.4% (348/862) of patients. Type III patients had significantly greater gestational age, gestational mass diameter, and preoperative serum β-HCG levels compared with type I and type II patients (all P<0.001). There was no statistically significant difference in the incidence of ultrasound-detected fetal cardiac activity among the three types of CSP patients (P=0.499).

Regarding treatment, 16% (138/862) of patients required adjuvant embryocidal therapy with intramuscular methotrexate (MTX) or oral mifepristone before or after surgery, with a significantly higher medication rate in type III patients compared with the other two groups (P<0.001). Among type II patients, 22.3% (102/458) required ultrasound-monitored surgery, which was higher than the other two groups (P<0.001). Among type III patients, 33.7% (30/89) required laparoscopic monitoring during surgery, which was higher than the other two groups (P<0.001). Overall, 17.5% (151/862) of CSP patients required uterine artery occlusion (uterine artery embolization or laparoscopic/open uterine artery blockage), with the rate being significantly higher in type III patients compared with type I and type II groups (P<0.001). The primary surgical approach for type I and type II patients was hysteroscopic gestational mass removal, while for type III patients it was primarily laparoscopic or open excision of gestational mass with uterine repair, although 34.8% (31/89) of type III patients could still undergo hysteroscopic gestational mass removal. Postoperative intrauterine balloon tamponade for hemostasis was required in 23.3% (201/862) of patients. Type III patients had significantly longer operation duration, greater 24-hour postoperative accumulated bleeding volume, higher incidence of bleeding $ $200 mL and blood transfusion rate, longer hospitalization duration, and higher treatment costs compared with the other two groups (P<0.001) .

The incidence of persistent CSP was 3.1% (27/862) among all CSP patients, with a higher incidence of 4.1% (19/458) observed in type II patients. There was no statistically significant difference in the incidence of persistent CSP among the three groups (P=0.187) .

Discussion

CSP is a special type of ectopic pregnancy in which the gestational sac implants in the uterine scar from a previous cesarean section [1]. Due to variations in cesarean scar defect (CSD) morphology, growth direction and invasion depth of the gestational mass, and degree of local vascularization, there is considerable heterogeneity in disease severity among different cases. Therefore, a rational classification system for CSP is of great significance for guiding clinical tiered management.

Vial et al. [12] first proposed the traditional dichotomous classification of CSP in 2000, dividing it into endogenic and exogenic types. Kaelin et al. [13] further clarified the two types based on the thickness of the myometrium between the gestational sac and bladder ($ $2-3 mm for endogenic type, <2 mm for exogenic type). Lin et al. [14] distinguished type I from type II based on whether the depth of gestational sac embedding into the scar reached half the thickness of the adjacent uterine wall, defined type III as gestational sac protrusion toward the bladder, and type IV as vascular-rich amorphous mass. Kang et al. [15] proposed a 3-type, 7-level clinical classification system by comprehensively quantifying CSD severity, gestational sac size and growth direction, and local blood flow characteristics. The 2016 CSP Chinese Expert Consensus [4] proposed classification into types I, II, and III based on ultrasound imaging features such as the growth direction of the gestational sac and the thickness of the myometrium between the sac and bladder. This classification is widely applied in current clinical practice, but there has been no analysis or summary of the clinical characteristics of different types of CSP under this classification standard.

This study found that type III CSP patients had longer gestational age at diagnosis, larger gestational mass diameter, and higher serum β-HCG levels, which were accompanied by increased operation duration, surgical blood loss, hospitalization duration, and treatment costs, as well as greater demand for medical resources including laparoscopic monitoring, uterine artery occlusion, more invasive surgical approaches (laparoscopic/open surgery), and blood products. Among type I and type II patients, those with gestational age $ $8 weeks accounted for only 21.0% (66/315) and 24.2% (111/458), respectively, while this proportion was 48.9% (43/89) in type III CSP patients. Based on this observation, two hypotheses can be proposed: (1) Type III CSP patients have more insidious onset, leading to later presentation at hospital. However, this study found no significant difference in clinical symptoms (abdominal pain, vaginal

bleeding) among different types of patients, making this hypothesis unlikely. (2) CSP classification may evolve dynamically with gestational age, with some type II or type I patients progressing to type III as gestational age increases [18]. Due to ethical considerations, this hypothesis is difficult to verify through clinical observation studies and can only be explored through imaging changes in the few patients who request expectant management or continuation of pregnancy.

Previous studies have suggested that CSP occurrence is associated with age, pregnancy interval, uterine cavity surgery history, number of cesarean sections, and timing of cesarean section, with $ $2 previous cesarean sections and post-cesarean uterine cavity surgery being strong risk factors [11]. This study compared these factors among different classification groups and found no statistically significant differences, indicating that risk factors for different types of CSP require further exploration. Other studies have summarized risk factors for CSD, which is a prerequisite for CSP and one of the reference factors for classification [16-17], but there is still a lack of research on the correlation between CSD risk factors and CSP classification types. Further data accumulation is needed to analyze the correlation between specific details of previous cesarean sections, such as perioperative complications, uterine incision suturing conditions (suture type, number of layers, myometrial suturing method), and CSP classification types.

Comprehensive management of CSP involves multidisciplinary team participation from obstetrics and gynecology, ultrasound, radiology, interventional vascular surgery, anesthesiology, and transfusion medicine, with more severe types requiring greater medical resources. The 2016 CSP Chinese Expert Consensus [4] recommends that type II, type III CSP, and type I CSP with gestational age $ $8 weeks should first undergo prophylactic UAE before ultrasound-monitored uterine evacuation. In this study, only 21% (96/458) of type II patients received uterine artery occlusion assistance before hysteroscopic gestational mass removal or uterine evacuation, but surgical blood loss and persistent CSP incidence were not increased compared with previous studies reporting uterine artery occlusion treatment [19]. This may be because most patients in this study were diagnosed and treated early, suggesting that the application of uterine artery occlusion should not be based solely on disease classification but should be decided in combination with gestational age, serum β-HCG level, TVUS or MRI imaging features, and patient fertility requirements to reduce complications associated with uterine artery occlusion techniques [20-22]. Type III patients have greater treatment complexity and higher complication risk, and should be actively referred to regional medical centers with extensive treatment experience.

Previous studies have reported that the incidence of persistent CSP after initial diagnosis and treatment ranges from 4.35% to 6.00% [23-25]. The incidence of persistent CSP in this study was 3.1%, with a higher rate of 4.1% observed in type II patients. The primary surgical approach for type III patients was laparoscopic or open excision of gestational mass with uterine repair, which had a high lesion clearance rate, while type II patients primarily underwent hysteroscopic

gestational mass removal, which was less invasive. However, because type II patients have thinner myometrium at the cesarean scar site and wider CSD, there may be blind spots under hysteroscopy. Therefore, comprehensive analysis of imaging features and strict surgical indications are necessary before surgery to reduce the incidence of persistent CSP.

This study comprehensively analyzed the clinical characteristics of different types of CSP patients and found that different types require different clinical priorities and medical resources, emphasizing the importance of early diagnosis and early treatment, which has important reference value for current clinical practice. Based on a large sample of cases from the National Clinical Research Center for Obstetrics and Gynecology Diseases and Beijing Critical Maternal Referral Center, this study has good universality and generalizability due to its wide patient source and balanced type distribution. However, this study has limitations as a single-center study with inherent retrospective bias. Further accumulation of case data is needed to comprehensively understand disease characteristics and make necessary supplements and improvements to the CSP classification system to better guide clinical management.

Author Contributions: WANG Chao and HOU Zheng conceived the study and designed the research protocol. WANG Chao was responsible for data collection, cleaning, statistical analysis, chart preparation, and drafting the manuscript. LI Huajun, LI Rong, and QIAO Jie revised the manuscript, provided quality control, and supervised the study. LI Huajun takes overall responsibility for the article.

Conflict of Interest: The authors declare no conflict of interest.

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