

# Treatments of caesarean scar pregnancy and the corresponding results in ten years

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**Abstract. – OBJECTIVE:** The purpose of this essay is to explore the treatments of caesarean scar pregnancy and the corresponding results during the past ten years.

**PATIENTS AND METHODS:** There were 56 cases of caesarean scar pregnancy in the past ten years which were divided into two groups. Group A included 22 cases in the first five years from January 2004 to December 2008, and group B had 34 cases in the last five years from January 2009 to December 2013. Analysis and statistical treatments are performed according to the comparison of the general state, severity, therapeutic condition and results in both groups.

**RESULTS:** We found that the operation rate of group A is lower than that of group B while the average hospitalization and follow-up time of group A are longer than that of group B. The re-hospitalization rate of group A is 22.73% (5/22) and is higher than 11.76% of group B (4/34). The vagina bleeding rate of group A is 27.27% (6/22) and is higher than 2.94% of group B (1/34).

**CONCLUSIONS:** With the increasingly deep-rooted concept of minimally invasive technique in gynecology, minimally invasive therapy becomes increasingly popular for the treatment of caesarean scar pregnancy. The advantages include short treatment period and follow-up time and safe therapy which to some extent reduces the burden and mental pressure of patients.

*Key Words:*

Caesarean scar pregnancy (CSP), Methotrexate, Lesions, Results.

## Introduction

Caesarean scar pregnancy (CSP) occurs when the implantation site of the gestation or embryo sac is on the caesarean scar that may cause the placenta increta, uterine rupture, massive haemorrhage, or even death. Although it was somewhat rare in the past, the incidence of CSP has recently increased due to the increase of the

caesarean section. Without timely clinical treatment, CSP may cause damage to the patients and even death. This study analyzes the 56 clinical cases of CSP after caesarean section during the past ten years between the early of 2004 and the end of 2013 in our hospital.

## Patients and Methods

Through data collection, 56 patients were diagnosed with CSP during the period of ten years from January 1994 to December 2003 in our hospital. There were 22 cases between January 2004 and December 2008, and 5328 gynecological hospitalized patients in synchronization, with the constituent ratio of 0.4%. There were 34 cases between January 2009 and December 2013, and 8012 gynecological hospitalized patients in synchronization, with the constituent ratio of 0.4%.

Twenty-two previous CSP cases between January 2004 and December 2008 were chosen as group A and the 34 cases between January 2009 and December 2013 as group B. The comparative analysis and statistical treatment were made mainly according to several factors such as the general information, severity, therapeutic condition, and results. The general conditions of these two groups such as age, gravidity and parity history, patients suffering from abdominal pain and the number of patients whose level of  $\beta$ -hCG in blood is higher than 10000 mIU/ml (human chorionic gonadotropin- $\beta$ ,  $\beta$ -hCG) before treatment are displayed in Table I. There was no statistically significant difference ( $p > 0.05$ ).

## Diagnostic Standard

The diagnosis is based on inspections on menolipsis, the level of  $\beta$ -hCG in blood, history of the caesarean section, ultrasound examination<sup>1</sup> and magnetic resonance imaging (MRI)<sup>2</sup>. Ultra-

**Table I.** Comparison of two groups before treatment.

Group	Age	Gravidity and parity history	Patients suffering from abdominal pain	The level of $\beta$ -hCG in blood >10000miu/ml before treatment
Group A (n = 22)	31.86 $\pm$ 5.37	4.18 $\pm$ 1.74	10	5
Group B (n = 34)	32.41 $\pm$ 5.05	4.12 $\pm$ 1.53	19	7
<i>t</i> ( $\chi^2$ )	0.387	0.145	0.582*	0.204*
<i>p</i>	0.700	0.855	0.446	0.886

Note: \*means  $\chi^2$

sound diagnostic standards<sup>1</sup>: (1) There is no gestation sac in the uterine cavity and the cervix. (2) Gestation sac or mass is located in the isthmus of the uterus anterior wall or the caesarean scar. (3) The lower segment muscular layer of the uterus anterior wall between the gestation sac or mass and the bladder becomes thinner or interrupted continually. (4) Prominent ring flow signal is found around the gestation sac or mass by Doppler Color Flow Imaging and Pulse Doppler shows the flow image with high speed (peak velocity > 20 cm/s) and low resistance (pulsatility index < 1), similar as that of the normally early pregnancy. (5) No mass is found in the adnexa area, and also no free liquid wave in Douglas cul-de-sac (except for the break of CSP). The relation between caesarean scar and gestation sac and the actual distance between the gestation sac and the uterus serous layer can be seen from the sagittal T2 weighted images of MRI<sup>2</sup>. The diagnosis can be made only when all the indexes above coexist.

### Treatment Methods

The CSP treatments can be classified into two types such as conservative treatment and surgery.

- 1. Conservative treatment using MTX Systemic Therapy and Methotrexate.** Eighteen patients in group A, were injected with methotrexate MTX 50 mg/m<sup>2</sup> in the bilateral deep muscle of the hip on the 1<sup>st</sup>, 3<sup>rd</sup>, 5<sup>th</sup> and 7<sup>th</sup> day, and also the Tetrahydrofolate (CF) 6 mg twice a day. Meanwhile, Mifepristone 50mg was administered three times a day on the 2<sup>nd</sup>, 4<sup>th</sup>, 6<sup>th</sup> and 8<sup>th</sup> day, 15 days as a course of treatment. The level of  $\beta$ -hCG in blood was reexamined and observed every two days.
- 2. MTX 100 mg was injected into the local lesions in the vagina by the leading of color Doppler ultrasound.** After the surgery, preventive use of antibiotics were given for 24 hours and CF 6 mg was injected 12 hours later after the surgery.

### Operative Treatment

Method 3: Lesion resection of the uterine with hysteroscopy and laparoscopy+ repair operation of the caesarean scar. With the epidural block anesthesia gave continually, and laparoscopy was used for inspection. For the surgery, dilate the cervix to 9-10 mm, move the hysteroscopy into the cervix internal orifice, observe and decide on the state of the lesion and explore the gestation sac. Use the unipolar cut mirror if the gestation sac protrudes outside with the cutting power 65-80 W, and coagulation power 30-40W. Cut the lesions of the gestation sac, and have the electric coagulation towards the bleeding points. If the gestation sac grows towards the reverse direction of the bladder and protrudes towards the uterus serous layer, no prominent gestation sac is seen under the hysteroscopy. Separate and push down the vesicouterine fold of the peritoneum of the bladder and find the lesions in the low segment of uterine, hold the uterus by uterine manipulator if necessary, and continuously suture the myometrium.

Method 4: Removal of the embryo by cutting the vagina and uterine + repair operation of the caesarean scar. Ways: in lithotomy position, patients are given epidural block anesthesia continually, with disinfection of the vulva and vagina, urethral catheterization and emptying the bladder. Then, using the forceps holder pull the cervical front lip and separate by water pressure the pituitrin diluent in the interval between the vagina and the bladder, incising the anterior wall of vagina horizontally and pushing the bladder to the fold of the peritoneum. Then, the lower segment lesions of uterine can be seen. If the lesion protrudes towards the uterus serous layer with violet color, inject 6 U pituitrin and incise the lesion horizontally or longitudinally, and use the forceps holder to lead and clear the gestation sac. Then, hold the uterine margin and curette the cervix and margin and prune the margin until the

**Table II.** Comparison of two groups for treatment.

Group	Cases	Conservative Treatment Cases		Operation Treatment Cases	
		Method 1	Method 2	Method 3	Method 4
Group A	22	14	5	3	0
Group B	34	6	12	11	5
$\chi^2$		6.656		6.656	
$p$		0.010		0.010	

myometrium can be seen. Suture the uterine margin with No. 0 micro-Joe line, close the peritoneum and suture the anterior wall of the vagina by 2-0 micro-Joe line.

**Criteria for Recovery**

The clinical abdominal pain and discomfort of the lower abdomen will disappear. The bleeding of vagina stops and the level of  $\beta$ -hCG in the blood decreases to the normal level. The mass disappears under color Doppler ultrasound inspection.

**Statistical Analysis**

Statistical analysis will be made through the software of SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Measuring of data are treated with Mean Standard Deviation ( $\pm s$ ), and comparison will be examined with  $t$ -test, and the counting materials will be examined with  $\chi^2$  test. The difference ( $p < 0.05$ ) has the statistical significance.

**Results**

**Treatment Comparison of Two Groups**

Selections of two projects of treatment are displayed in Table II. The selection of conservative treatment is more than that of the last five years while the selection of the operation is more than that of the first five years. Such difference is statistically significant ( $p < 0.01$ ).

**Results of Two Groups**

In group A, there are four cases whose clinical symptoms and local lesions disappear under the color Doppler ultrasound and no follow-up is made with the cases whose level of  $\beta$ -hCG in blood is less than 100 mIU/ml. In group B, six cases are not followed up, and the other cases are all cured. The hospitalization time of group A is around 6-14 days and five cases are re-hospitalized due to the CSP, while the average hospitalization time of group B is about 5-14 days and four cases are re-hospitalized due to the same CSP. The differences in the comparison are statistically significant ( $p < 0.01$ ). Except for the cases failing to follow-up, we compare the other cases in two groups after clinical therapy. The time that the level of  $\beta$ -hCG in the blood of can be reduced to the normal level in group A is from the shortest 17 days to the longest 100 days with the average  $47.56 \pm 25.19$  days. The time that the level of  $\beta$ -hCG in the blood of can be reduced to the normal level in group B is from the shortest 12 days to the longest 92 days with the average  $32 \pm 12.96$  days. The comparison is significantly different ( $p < 0.01$ ). The time that the local lesions disappear in group A is, from the shortest 14 days to the longest 82 days, with the average  $38.23 \pm 17.04$  days. The time that the local lesions disappear in group B is from the shortest 10 days to the longest 82 days with the average  $33.53 \pm 16.98$  days. The comparison is not significantly different ( $p > 0.05$ ). The statistical re-

**Table III.** Comparison of treatment results in two groups.

Group	Average hospitalized time (d)	Time of GS to disappear (d)	Time of $\beta$ -hCG in blood to the normal level (d)
Group A	11.59 $\pm$ 4.15	38.23 $\pm$ 17.04	47.56 $\pm$ 25.19
Group B	8.24 $\pm$ 2.66	33.53 $\pm$ 16.98	32.00 $\pm$ 16.96
$t$	3.693	1.010	2.324
$p$	0.001	0.317	0.028

sults can be seen in Table III. Moreover, there are six cases in 22 due to the massive bleeding for once, amounting to 1000-2000 ml, who get the UAE therapy; one case suffers the massive bleeding for once in group B, amounting to 1200 ml, who get the synergic UAE therapy. The comparison is significantly different ( $p < 0.05$ ). One in five re-hospitalized cases in group A gets the MTX chemotherapy again, two cases are re-hospitalized due to the myelosuppression, and one case due to massive vaginal bleeding and one case due to the abdominal pain after MTX chemotherapy; among four re-hospitalized cases, two are re-hospitalized due to the massive vaginal bleeding, one case due to the oral ulcer and one case due to the abdominal pain perhaps after hysteroscopy and laparoscopy treatment.

## Discussion

Recently with the increase of caesarean section rate worldwide, the prevalence rate of CSP also raise a lot. There is no accepted CSP treatment method yet and also no unified and exact treatment project due to the relatively low incidence rate of CSP and lack of enough knowledge and strong medical evidence. The state of illness or the improper treatment may cause uterine perforation, massive bleeding or even death. Therefore, the diagnosis should be made in order to choose the appropriate treatment. The features and selections of different CSP treatments are discussed as below.

Methotrexate (MTX) is used quite often in systemic and local chemotherapy. Methotrexate is a quite an effective folic acid antagonist whose effect has been recognized in the treatment of ectopic pregnancy<sup>3</sup>. The effect has been proven<sup>4</sup>, when the dosage is 1 mg/kg or 50 mg/m<sup>2</sup> for the systemic medication of ectopic pregnancy and the dosage is counted by 1 mg/kg for the systemic treatment of CSP after caesarean section every 4 days, 0-8 days a course. The decision whether to reuse the MTX or not should depend on the HCG level in blood and the inspection result of the color Doppler ultrasound<sup>5</sup>. It is noteworthy that failure to cure the CSP may cause the patients to suffer the uterine rupture or massive or repeating vaginal bleeding. Therefore, special attention should be given to the selection and inspection during the treatment process. Now, no CSP chemotherapy index can be relied on but the indexes of ectopic pregnancy: (1)

MTX systemic medication therapy is effective when the level of  $\beta$ -hCG in the blood is less than 5000 mIU/ml; MTX systemic medication therapy combined with local or repeated medication, when the level of  $\beta$ -hCG in blood is more than 6000 mIU/ml; (2) continually with assisted curettage therapy after the surgery<sup>6</sup>. If the ultrasound shows that high speed and low resistance of the artery blood flow spectrum occurs in the gestation sac, or the level of  $\beta$ -hCG in the blood increases during the treatment process, be cautious of uterine rupture and the erosion of embryo. We can find in the treatment process, that the level of  $\beta$ -hCG in the blood needs a long time to decrease, with the longest time reaching more than three months and the disappearing time of gestation sac reaching 2-3 months. This is basically identical to the observation of Muraji et al<sup>7</sup> that it generally takes 4-17 weeks for the level of  $\beta$ -hCG in blood to come back to normal after medication, 12-17 weeks for the gestation sac to disappear entirely<sup>7</sup>. According to this research MTX, chemotherapy cases in the first five years are more than that in the last five years. Compared with the incision of local lesions from the surgery, MTX chemotherapy is featured with the long time follow-up and risk of massive bleeding. Remarkably, four cases in total from the nine re-hospitalized cases in the two groups had side effects from the MTX chemotherapy. Therefore, side effects of MTX chemotherapy should monitor the medication and follow-up process and be dealt with properly.

Local lesions resection and surgical repair of the uterine. In the past, local lesions resection was considered when the conservative treatment failed, or the hemodynamics of the patients were unstable. Through our research, diagnosed CSP patients in the early stage can have the local lesion resection and surgical repair of the uterine by lesion resection on the caesarean scar via the abdomen, vagina and uterine, or lesion resection on caesarean scar with hysteroscopy and laparoscopy. The surgical method used is related to the clinical experience of the surgeon, the state of hemodynamics of patients and whether the gestation sac is adhered with the bladder through the cesarean scar. Combined detection of hysteroscopy and laparoscopy can provide the exact diagnosis of the scar pregnancy. Hysteroscopy and laparoscopy results in less bleeding and quick recovery but is quite expensive. Transvaginal CSP debridement surgery is a newly-type treatment that can remove the lesions entirely with little dis-

turbance to the abdominal viscera<sup>8</sup>. There is little incidence rate of intestinal obstruction after the surgery by which the intestinal function of the patients can recover quickly, lowering the burden of expense. Natural orifice transvaginal caesarean scar debridement is minimally invasive surgery with less trauma and quicker recovery period so that patients can take care of themselves better. Transvaginal caesarean scar debridement is featured with the low infection rate, small requirement towards the antibiotics and painkiller, reduction of hospitalized time and no scar left after the surgery.

Based on this research, we find that the local lesions resection of caesarean scar whether through hysteroscopy and laparoscopy both have the advantages of short hospitalized and follow-up time. Because only five patients in the recent five years accepted the removal of the embryo by the cutting of the vaginal and uterine+ repair surgery of the caesarean scar, further clinical research is needed.

Moreover, uterine artery embolization, results from massive bleeding of CSP patients. Uterine artery embolization is one of the fastest ways to hemostasis massive bleeding<sup>9</sup>. This contributes to keeping the uterine and reproductive ability. Uterine artery embolization is the backup for successful treatment of CSP. If no such condition is offered, please transfer to another available hospital in case of the following medical dispute.

### Conclusions

Once the pregnancy is diagnosed in women who have a history of caesarean section, they should accept the ultrasonography to eliminate the possibility of CSP, whether they have symptoms such as vaginal bleeding or not. If they suspect having CSP, patients should be hospitalized as soon as possible. MRI inspection is suggested in order to diagnose the size of lesions and judge the severity. Among several

feasible treatments, the most economical way will be chosen based on the specific situation of the department and the current operative conditions.

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### Conflict of Interest

The Authors declare that they have no conflict of interests.

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