Caesarean scar pregnancy - Is there a light in the end of the tunnel?

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Research Article

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Abstract

**Purpose:** to summarize and present a single tertiary center’s 25 years of experience managing patients with caesarean scar pregnancies and their long term reproductive and obstetric outcomes.

**Methods:** A 25-year retrospective study included women diagnosed with CSP from 1996 to 2020 in one tertiary center. Data were retrieved from the medical records and through a telephone interview. Diagnosis was made by sonography and color Doppler. Treatments included methotrexate, suction curettage, hysteroscopy, embolization and wedge resection by laparoscopy or laparotomy as a function of the clinical manifestations, the physicians’ decisions, patient counseling, and parental requests.

**Results:** Analysis of the records recovered 60 cases of CSP (two of whom were recurrent). All patients had complete resolution with no indication for hysterectomy. Thirty-five patients had a long-term follow-up, of whom 24 (68.6%) attempted to conceive again and 22 (91.6%) succeeded. There were 17/22 (77.3%) patients with at least one live birth, 3/22 (13.6%) spontaneous miscarriages and 2/22 (9%) recurrent CSP. The obstetric complications included abnormal placentation 5/19 (26.3%), premature rupture of membranes 2/19 (10.5%), preterm delivery 4/19 (21%) and abnormality of the uterine scar 2/19 (10.5%). There was one case of neonatal death due to complications of prematurity 1/19 (5.2%).

**Conclusion:** CSP treatment focusing on reducing morbidity and preserving fertility has favorable long term reproductive and obstetric outcomes. In subsequent pregnancies, we recommend performing an early first trimester vaginal scan to map the location of the new pregnancy, followed by close monitoring given the obstetric complications mentioned above.

Introduction

Cesarean scar pregnancy (CSP) is an iatrogenic complication that constitutes a life-threatening condition [1, 2]. The incidence reported in recent studies ranges from 1:1800 to 1:2500 of all cesarean deliveries performed [3–6]. The incidence of CSP appears to be on the rise. This trend can be explained by the increase in the rate of cesarean deliveries, but also by the increase of the use of trans-vaginal-soundoscopy (TVS) and clinical awareness [7, 8]. Although CSP is considered to be a form of ectopic pregnancy it shares its etiology with early placenta accreta [9, 10]. There are two forms of CSP: Type 1 (on the scar) where the pregnancy develops towards the uterine cavity, and Type 2 (in the scar) where the pregnancy develops toward the urine bladder [11].

Four main treatment options are described in the literature [12, 13]:

**Medical treatment** – the most common treatment is methotrexate (MTX), given locally, systemically or in combination.

**Invasive radiology** - uterine artery embolization

**Sonographic treatment** - high intensity focused ultrasound.
Surgical procedures – dilation & curettage (D&C), hysteroscopy, colpotomy, laparotomy or laparoscopy.

To date, there is no consensus as to the optimal treatment. Hence, treatment is tailored according to the clinical manifestations, and the experience and abilities of the medical institution.

Expectant management of viable CSP may be life-threatening to both the mother and the fetus, and other complications can arise, such as early uterine rupture, invasive placentation, severe blood loss, preterm delivery, and future infertility mainly due to hysterectomy \([6, 12, 14–16]\). Nevertheless, in recent years there have been a growing number of reports of expectant management of viable CSP some of which resulted in a live birth, even in late preterm or term. Most of these cases required surgical intervention, including hysterectomy, leading to loss of further fertility \([6, 8, 12, 14–16]\). The reproductive outcomes reported in the literature after treatment for CSP are encouraging but are limited given the rarity of this condition. The majority of patients who were managed without a hysterectomy were able to conceive again and the reported risk for recurrent CSP was low \([2, 17, 18]\). The goal of the current study was to present our extensive (> 25 years) experience managing patients with CSP and their long-term follow-ups in terms of their reproductive and obstetric outcomes.

Materials And Methods

This retrospective study included women who were diagnosed with CSP in Shamir (previously Assaf-Harofeh) medical center in Israel. The data were retrieved from the hospital medical records. Diagnosis of CSP was based on abdominal and transvaginal ultrasound. The sonographic criteria for diagnosis were \([1, 8, 19-23]\) as follows:

1. An empty uterus
2. An empty cervical canal
3. Location of the gestational sac in the anterior part of the isthmic portion of the uterus with a diminished myometrial layer between the bladder and the sac
4. Evidence of a discontinuity in the anterior wall of the uterus on the sagittal view of the uterus when the direction of the ultrasound beam runs through the amniotic sac.
5. Doppler demonstration of a rich vasculature in the area of the cesarean scar.

Treatment:

The MTX dosage for intramuscular injection was 50 mg/m\(^2\) (based on calculated body surface area). Fixed dose of 25 mg of MTX was used for local injection to the gestational sac. Repeated doses of systemic MTX were given according to bHCG levels and sonographic findings during the follow-up. In all cases of hemodynamic instability, a laparotomy was performed. In patients who preferred surgical treatment as the first line, a wedge resection under laparotomy or laparoscopy was performed. The long-term follow-up analysis was based on a review of hospital medical records and telephone
interviews. Collected data included the patients` family planning, reproductive and obstetric outcomes in subsequent pregnancies.

This study was approved by the Institutional Review Board (0281-16-ASF)

**Results**

Sixty cases of CSP in 58 women were diagnosed in our department from 1996 to 2020 with an average age of 35.5 years (range, 25–44 years). The median number of previous pregnancies was 5 (range 2–18), the median number of previous deliveries was 2 (range 1–7) and the median number of previous cesarean sections was 2 (range 1–4). Two patients had previous CSP. The management and treatment flow chart is presented in Fig. 1. For purposes of the current study the patients were divided into 2 groups according to the conceptus viability (i.e., cardiac activity) of the pregnancy: Group A was composed of 29 cases with cardiac activity (viable) and Group B was composed of 31 cases without cardiac activity (non-viable).

**Group A (viable pregnancy) management**

Twenty-three out of the 29 patients (79.3%) were treated with MTX, of whom 19 (82.6%) had complete resolution. Two patients (8.7%) needed an intervention with suction curettage due to suspected retained products of conception. In two other patients (8.7%) the CSP did not resolve after repeat doses of systemic MTX, and on sonography the gestational sacs demonstrated enhanced myometrial vascularity on the Doppler scan. Along with the sonographic appearance, their bHCG levels did not decrease. These patients had further treatment with selective embolization. One of them had clinical and sonographic resolution. The other needed hysteroscopic removal of the retained products of conception.

Two patients out of 29 (6.9%) had a laparotomy since both preferred surgical intervention over MTX, and underwent wedge resection. One patient had completed her family planning and requested tubal sterilization during the same procedure.

Three patients out of 29 (10.3%) underwent primary suction and curettage. Two patients were misdiagnosed as having an intra uterine pregnancy implantation before the procedure. One patient was referred to the emergency room (ER) with vaginal bleeding and was misdiagnosed as early inevitable abortion. During the procedure increased vaginal bleeding occurred. Arteriovenous malformation (AVM) was suspected but was not found in the angiography. The bleeding was resolved by local intracervical injection of Vasopressin. She was discharged for further follow-up. A week later she was readmitted due to excessive vaginal bleeding. In a repeat angiography, AVM was diagnosed and embolization was performed. Two days later during hospitalization, excessive bleeding again occurred, and this time, the diagnosis of retained products of conception in the cesarean scar after CSP was made. She was taken to surgery. Upon hysteroscopy, an amorphic tissue was observed in the niche, and no myometrium tissue was seen between the niche and the bladder. After switching to laparoscopy, a wedge resection was performed successfully.
The second patient had suction curettage for termination of pregnancy. During the procedure, increased bleeding occurred. CSP was suspected and the operating team switched to laparotomy which confirmed the diagnosis. Wedge resection was completed uneventfully.

One patient was offered treatment with MTX, but opted for expectant management. She was lost to follow until 24 weeks of gestation, when she presented at the ER in a state of hypovolemic shock. She had an emergency laparotomy in which uterine rupture was diagnosed. The fetus did not survive, but the uterus was preserved.

**Group B (non-viable pregnancy) Management**

Nineteen patients out of 31 (61.3%) were treated with MTX. Fifteen patients (78.9%) had resolution with no further treatment. One patient (5.3%) needed suction and curettage after she was diagnosed with incomplete abortion. Another patient (5.3%) who was treated with MTX had a rise in bHCG a week later. In the follow-up ultrasound, a gap was revealed in the myometrium above the pregnancy sac. A wedge resection was performed during laparotomy. Two patients (10.5%) who were treated with MTX later underwent embolization. One had increased vaginal bleeding after the MTX treatment. Embolization was performed followed by laparotomy due to increased vaginal bleeding. A CSP involving the bladder was observed and wedge resection was performed. The other patient was suspected of having an AVM and her bHCG was in plateau. After embolization her bHCG level decreased and she underwent suction curettage after sonography identified a remaining gestational sac.

Six patients out of 31 (19.3%) were treated primarily with suction and curettage. Three needed no further treatment. The other three patients were misdiagnosed as intra uterine missed abortion. All had massive vaginal bleeding during the elective procedure. In two patients, sonographic suspicion of CSP led to conversion to emergent laparotomy. CSP was diagnosed and resected while preserving the uterus. The third patient was managed by systemic and local uterotonics and Tranexamic acid. Since the bleeding resolved, she was then managed by conservative follow-up and hysteroscopic repair of the cesarean scar niche.

Two patients out of 31 (6.4%) underwent primary hysteroscopy. They were suspected of having retained products of conception after missed abortion. In hysteroscopy the tissue was shown to be embedded in the niche of the cesarean scar. One was treated with methotrexate. Later on, they both underwent embolization due to AVM. Subsequently they underwent another hysteroscopy in which removal of the retained tissue was performed successfully.

Four patients out of 31 (12.9%) were managed expectantly with no complications.

**Long term follow-up**

The long-term follow-up flow chart is presented in Fig. 3. Thirty-three patients with 35 cases of CSP were followed-up. Eighteen out of 60 were lost to follow-up, one patient had tubal sterilization and 6 were recent cases. The median follow-up period was 3.8 years (range 0.5–22 years).
Reproductive outcomes (Fig. 3)

Twenty-four patients hoped to conceive again, of whom 22 (91.6%) were successful. Of these, 19 (86.4%) women conceived spontaneously. Three patients conceived more than once. Three patients had a spontaneous early abortion (13.6%), and two patients (9%) had recurrent CSP. Seventeen patients (77.3%) had a live birth. There was one case of neonatal death due to prematurity complications. Two patients had two live births. The mean gestational age at the time of delivery was 36.5 weeks (range 25–41). There were 4 (21%) preterm deliveries. Sixteen (84.2%) patients delivered by repeat cesarean section. Ten (62.5%) were planned and 6 (37.5%) were emergent. Two (11.7%) patients had a vaginal birth.

Pregnancy and obstetric outcomes (Table 1) Five out of 19 (26.3%) pregnancies were complicated with abnormal placentation, 3 pregnancies with placenta accreta, one placenta previa and one patient had retained products of conception complicated with endometritis. One patient (5.3%) was delivered at 33 weeks of gestation by emergent cesarean section due to placental abruption. Two out of 19 (10.5%) pregnancies were complicated with preterm premature rupture of membranes (PPROM), one of whom, had partial placenta previa and was delivered by emergent cesarean section at 25 weeks of gestation due to fetal distress. Unfortunately, this ended with neonatal death in the neonatal intensive care unit (NICU). Two out of 19 (10.5%) pregnancies were complicated with cesarean scar abnormalities. One was delivered at 37 weeks of gestation by planned cesarean section in which a small uterine rupture was diagnosed. The second patient was delivered at 32 weeks of gestation by emergent cesarean section due to painful cesarean scar. Dehiscence was observed.
Table 1
Pregnancy and obstetric outcomes following CSP

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Mode of Conception</th>
<th>Pregnancy Outcome</th>
<th>Mode of Delivery</th>
<th>Gestational Age at The Time of Delivery</th>
<th>Pregnancy Complications</th>
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</thead>
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<tr>
<td>3</td>
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<td>CSP</td>
<td></td>
<td></td>
<td></td>
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<td>spontaneous</td>
<td>miscarriage</td>
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<td></td>
<td></td>
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<td>CSP</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Ovulation induction</td>
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<td>40</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IUI live birth planned CS 38</td>
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<td>miscarriage</td>
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<td></td>
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<td></td>
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<td>live birth</td>
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<td>urgent CS</td>
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<td>27</td>
<td>spontaneous</td>
<td>live birth</td>
<td>planned CS</td>
<td>37</td>
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</tr>
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</table>

IUI - intra uterine insemination
IVF - in vitro fertilization
CS - caesarean section
PROM - premature rupture of membranes
PPROM - preterm premature rupture of membranes
<table>
<thead>
<tr>
<th>Patient #</th>
<th>Mode of Conception</th>
<th>Pregnancy Outcome</th>
<th>Mode of Delivery</th>
<th>Gestational Age at The Time of Delivery</th>
<th>Pregnancy Complications</th>
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<tr>
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<td>spontaneous</td>
<td>live birth</td>
<td>urgent CS</td>
<td>32</td>
<td>cervical insufficiency, PPROM</td>
</tr>
<tr>
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<td>live birth</td>
<td>urgent CS</td>
<td>32</td>
<td>scar dehiscence</td>
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<tr>
<td>39</td>
<td>spontaneous</td>
<td>live birth</td>
<td>urgent CS</td>
<td>38</td>
<td>placenta accreta, PROM</td>
</tr>
<tr>
<td>41</td>
<td>spontaneous</td>
<td>miscarriage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>spontaneous</td>
<td>live birth</td>
<td>planned CS</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

IUI - intra uterine insemination

IVF - in vitro fertilization

CS - caesarean section

PROM - premature rupture of membranes

PPROM - preterm premature rupture of membranes

In terms of the risk for CSP based on the previous number of cesarean sections (CSs), our data for 2017–2020 indicate 6 cases of CSPs after one CSs, and 12 cases of CSs after 2 or more CSs. During the same period, we had 2744 deliveries after one CSs, and 1135 deliveries after 2 or more CSs. These led to OR = 4.84 (95% CI, 1.81–12.91) for CSP post one CS versus CSP post 2 or more CSs.

**Discussion**

This retrospective 25-year study revealed a rising trend in the rate of CSPs. A 2011 study conducted in our medical center on CSPs from 2000 to 2009 reported a prevalence of 1:3000 for the general obstetric population, and 1:531 among women who had undergone at least one cesarean delivery [2]. In the current
study the calculated prevalence for 2010–2020 was 1: 2132 for the general obstetric population, and 1:414 among women who had experienced at least one cesarean delivery. These findings also strengthen the assumption that the risk of CSP is related to the number of previous CSs, which here was OR = 4.84.

The diagnosis of CSP can be challenging, especially in early pregnancy. Misdiagnosis as an intrauterine pregnancy can lead to severe morbidity and mortality if curettage is performed or in cases of viable pregnancies. In this study, five patients were misdiagnosed with intrauterine pregnancy and underwent suction and curettage. All of them had excessive bleeding that led to further interventions including embolization, laparoscopy and laparotomy. AVM and excessive bleeding are a known complication of curettage in the presence of CSP [13, 24, 25].

There is no consensus as to the optimal treatment for CSP in the literature. Our policy involves offering medical treatment (MTX), and surgical treatment including laparoscopy, laparotomy and hysteroscopy, and invasive radiology (embolization) as primary or adjuvant therapy. Our treatment of choice is systemic MTX or combined systemic and local injection of MTX, depending on the clinical, sonographic and laboratory findings. In pregnancies with cardiac activity, we prefer to use the combined MTX treatment. In the cases of non-viable CSPs and spontaneous decrease in bHCG levels, we preferred expectant management.

Studies of reproductive outcomes present encouraging results in patients with SCPPs. Most women are able to conceive again after treatment for CSP [2, 17, 18]. The reported risk for recurrent CSP is low. Our experience further supports these findings.

The obstetric complications observed during the following pregnancies which resulted in live births included abnormal placentation (26.3%), preterm deliveries (21%) and one case of extreme prematurity and early neonatal death (5.2%) (see Table 1).

There are recent reports of expectant management of CSPs with cardiac activity. Trich et al. [8] reported ten patients with viable CSP managed expectantly. Four (40%) had a live birth by scheduled cesarean section at 32–36 weeks of gestation. Three of these patients (75%) underwent planned hysterectomies due to placenta previa percreta. Five out of 10 (50%) patients had adverse outcomes, and lost their pregnancies between 15–20 weeks of gestation, and all needed a hysterectomy (3 because of uterine rapture). Overall 8/10 patients had a hysterectomy. In a meta-analysis by Cali et al. in 2018 [14], 52 CSPs with cardiac activity were managed expectantly, and only 40/52 (76.9%) progressed to the 3rd trimester, with nearly 40% severe bleeding, 10% uterine rapture and more than 60% of the patients needed a hysterectomy during cesarean surgery. About 75% had an abnormal invasive placenta. No data were provided on neonatal outcomes.

The Glenn et al. [13] review summarized current management strategies for CSPs and found that expectant management in viable CSP entails a high rate of morbidity. In particular they noted that "more than 50% of patients having complications including hysterectomy, preterm deliveries, uterine rapture, significant hemorrhage and future infertility".
Recent reports distinguish between two types of CSP termed Type 1 (on the scar) and Type 2 (in the scar) CSP [11]. The prognosis for Type 1 CSP is considered favorable for live births in cases which are followed-up expectantly. Although Type 2 CSP has a higher risk for uterine rupture, both types of CSP have risks for severe invasive placentation which can also lead to massive blood loss and fertility loss. For these reasons we recommend treatment and termination of pregnancy to all of our patients with viable CSP. In our series, only one patient who had CSP with cardiac activity chose expectant management and declined to follow our recommendations. She presented later to the ER at 24 weeks of gestation in a state of hemorrhagic shock following uterine rupture, and her fetus did not survive.

In light of our experience and the recent literature we consider that expectant management is reasonable for non-viable CSPs, whereas termination of pregnancy is the best choice for viable CSPs. This approach can improve the long-term chances of fulfilling the patients’ desire for live births, while lowering the likelihood of complications in this dangerous scenario. Thus, when providing consultation to women with CSP, they should be made aware of the favorable outcomes of the subsequent pregnancy, after termination of the CSP.

**Research limitations**

This study utilized a retrospective design, therefore there could be no control of other associated factors. Records with incomplete data could not be completed. Some of the patients did not deliver in our medical center. In these cases, the data were based on a telephone interview. There was no comparison between patients and different kinds of treatments because there was no standardization of treatment or fixed management protocol. The treatment was tailored to the patient according to the clinical presentation as discussed above. We could not compare expectant management of viable CSP to termination of pregnancy as we strongly recommend against continuation of the CSP.

**Research strengths**

This study included a relatively large number of patients over a long follow up period in one tertiary medical center. In Israel there is a high birth rate and we were able to document a large number of repeat pregnancies.

**Conclusion**

The current findings support studies indicating an increase in the rate of CSPs in recent years. We also found that the risk for CSP is higher after repeat CSs. Health care providers should be aware of this type of ectopic implantation and be familiar with the different treatment options and the benefits and drawbacks of each of them. This study emphasizes the favorable long term obstetric and reproductive outcomes of early treatment of CSPs. These can be achieved with treatment focusing on fertility preservation. In subsequent pregnancies a higher risk for abnormal placentation should be expected. We now follow all our patients who have undergone a cesarean section (including post CSP) in a special clinic that offers them a pre-conceptual scan to assess the appearance of the uterine scar (niche) and a
5-7 week scan after conception to determine pregnancy implantation. Based on the above we advise each of our patients individually, and assess their need for close monitoring in high-risk pregnancy units to maximize a favorable obstetric outcome.

Declarations

Authors contribution:

Y Shiber - manuscript writing
R Maymon - manuscript editing
M Gal-Kochav - data collection
N Kugler - data collection
M Pekar-Zlotin - data collection
N Smorgick - manuscript editing
Z Vaknin - manuscript editing

Compliance with Ethical Standards

The authors declare no conflict of interest.

no funds, grants, or other support were received during the preparation of this manuscript. The authors have no relevant financial or non-financial interests to disclose.
This study was approved by the Institutional Review Board (0281-16-ASF).
Since this is a retrospective study, no informed consent was needed. Patients who were interviewed by the phone gave their informed consent verbally at the beginning of the survey.
The authors declare that the data supporting the findings of this study are available within the article.
Additional data are available by the corresponding author upon a reasonable request and subjected to the ethical standards and patients confidentiality.

Conflict of Interest Statement

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References


Figures
CSP - caesarean scar pregnancy; FH - fetal heart activity; MTX - methotrexate; SC - suction curettage

* The patient declined to follow recommendations for treatment / termination of pregnancy. She was lost to follow-up until 24 weeks of gestation, at which time she presented in a state of hypovolemic shock due to uterine rupture. See more details in the text.

Figure 1
Flowchart of CSP Patient Management and Treatment
Figure 2

Caesarean scar pregnancy ultrasound

A - Caesarean scar pregnancy in trans vaginal ultrasound

B - Trans vaginal ultrasound and color Doppler demonstrating rich vascularization in the caesarean scar

C - Trans vaginal ultrasound and color doppler of the same patient after systemic and local injection of methotrexate
Figure 3

Long Term Follow-up Flowchart