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Cesarean scar pregnancy (CSP) successfully treated with dilatation and curettage after failed local methotrexate treatment: A case report and updated mini-review

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Abstract

Background: Caesarean Scar Pregnancy (CSP) is a very rare form of an abnormal pregnancy that implants in a Cesarean section scar. The incidence is mainly increasing due to increasing number of Cesarean sections**.** This condition is associated with substantial morbidity and even mortality.

Case presentation: Because of its rarity, currently, there is no consensus on the preferred mode of treatment or follow up of CSP. Herein we report our experience with a case of first trimester CSP which was successfully managed with *dilatation*, *evacuation* and *curettage* (D&C), under ultrasound guidance, after failed local Methotrexate (MTX) treatment.

Mini review: We included an updated mini review of literature targeted for such lines of treatment (*local MTX* and *D&C*). The first authoritative recommendations on the CSP, by the Society for Maternal-Fetal Medicine, are summarized.

Conclusion: Operative intervention as D&C to treat CSP after failed local MTX treatment is a viable option characterized by technical simplicity efficacy and avoidable or controllable intra-operative complications. This is particularly justifiable if other advanced therapeutic techniques are not available**.**

Keywords: cesarean scar pregnancy; local methotrexate; dilatation and curettage.

Abbreviations: CSP: Cesarean Scar Pregnancy; CS: Cesarean Section; B-Hcg: The Serum Beta Human Chorionic Gonadotropin; US; Ultrasonography; TV/US: Transvaginal Ultrasonography; MRI: Magnetic Resonance Imaging; MTX: Methotrexate; KCL: Potassium Chloride; D&C: Dilatation And Curettage- UAE: Uterine Artery Embolization; SMFM: Society For Maternal-Fetal Medicine.

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Background

Historically, the pregnancy in a uterine scar saccule was first reported more than 40 years ago (in 1978) [1]. Nowadays, it is termed as Cesarean scar ectopic pregnancy (CSEP) or simply Cesarean Scar Pregnancy (CSP). It is associated with high morbidity and mortality [2]; therefore, accurate diagnosis and effective management are of major importance. Incidence rates of 1/1800–1/3000 pregnancies have been reported [3]. Generally, its incidence is probably increasing due to increasing rates of Cesarean Section (CS) and in-vitro-fertilization embryo- transfer [4]. Current evidence points to first trimester CSP as an entity in the continuum leading to morbidly adherent placenta and its substantial complications [5,6].

The pathophysiology of the CSP remains unclear, but the main mechanism is the invasion of a microscopic tract within the CS scar by the blastocyst as it implants [7]. Tissue fibrosis and poor wound healing are responsible for the formation of the defect in the Cesarean wound [8]. Actually, the CSP is similarly reported following a hysterotomy scar, metroplasty, myomectomy, uterine evacuation, previous abnormally adherent placentation, manual removal of placenta, hysteroscopy, and *in vitro* Fertilization (IVF) [4].

Because of its rarity, currently, there is no consensus on the preferred mode of treatment or follow up of CSP. Herein we report a case of first trimester CSP which was successfully managed with Dilatation, evacuation and Curettage (D&C), after failed local treatment with Methotrexate (MTX), under continuous transabdominal ultrasonographic guidance. Also, we included an updated mini review of literature targeted for such lines of treatment and the first authoritative recommendations on the CSP, by the Society for Maternal-Fetal Medicine, are summarized.

Case presentation

Demographic and clinical data

A 33-year-old woman (G6 P2+3) 2 livings, presented at the emergency department of Abha Maternity and Child Hospital, Abha, Saudi Arabia. She was complaining of amenorrhea of 7 weeks duration with vaginal bleeding and spotting few days ago. The patient reported a history of previous 3 first trimester spontaneous miscarriages followed by curettage and one emergency Cesarean delivery due to intrapartum fetal asphyxia, six years ago. She also reported no history of ectopic pregnancy, and had never used any contraceptive method. General examination revealed all vital signs were within normal. On abdominal examination, the abdomen was mildly tender with-out rebound tenderness. Vaginally, there was mild vaginal bleeding.

Diagnosis

Routine laboratory investigations including Liver Function Tests, Kidney Function Tests and Complete blood Count all were within normal. The serum beta-human chorionic gonadotropin (β-hCG) was 87,767 mIU/ml. Transvaginal Ultrasonography (TV/US) identified a gestational sac with a live embryo, at the isthmic region (within the Cesarean scar defect) with a crown to the rump length (CRL) of 68 mm (corresponding to the gestational age of six weeks and 5 days). A thin layer of myometrium separating it from the bladder was seen (~2.5 mm). The sac mainly grows toward the uterine cavity. Both the endocervical canal and the endometrial cavity were empty and the decidua measured 9 mm (*on a sagittal view*). (Figure 1) A functional trophoblast was demonstrated on color Doppler imaging studies. Both adnexa were normal and no free fluid was seen in the Douglas' pouch.

Intervention and outcome

The patient was counseled regarding the available management options of CSP including medical and surgical treatments with thorough explanations of advantages and disadvantages of each choice. Since all vital signs were stable, serum β-hCG was > 12,000 IU/L and the patient is young an attempt was made to institute conservative treatment and to preserve fertility. Thus the decision was taken to inject 1 ml of potassium chloride (KCL) into the fetal heart (to hasten embryo's demise) followed by 100 mg of Methotrexate (MTX) into the gestational sac, using the TV/US-guidance. Initial aspiration of the gestational sac amniotic fluid was done. There was no internal bleeding or lower abdominal pain noticed following the procedure. The patient was admitted to the ward for observation.

Day 4 post-TV/US guided treatment and MTX, her serum β-hCG was 86,193 m IU/ml, Day 7 (post treatment), the serum β-hCG was 81,165 m IU/ml; though the patient was stable but we were not satisfied with such a poor drop of the β-hCG level (<15% as per the American College of Obstetricians and Gynecologists (ACOG) guidelines) [9]. Finally, a decision was taken to give the patient misoprostol 400 µgm Q 8 hours vaginally and to perform *dilatation*, *evacuation* and *curettage* (D&C) under transabdominal US guidance. During the procedure the whole sac was removed without any complication, and the products were sent for histopathology.

After 48 hours of the D&C the patient serum β-hCG level dropped to 6,456 m IU/ml, and she was discharged home in a good stable condition. The patient was having a weekly serum β-hCG as an outpatient, a week later the patient came to the clinic with no complaint and her β-hCG dropped to 230 mIU/ml. Finally, a week after that the serum β-hCG value was negative. The patient was advised to avoid a subsequent pregnancy for at least six months.

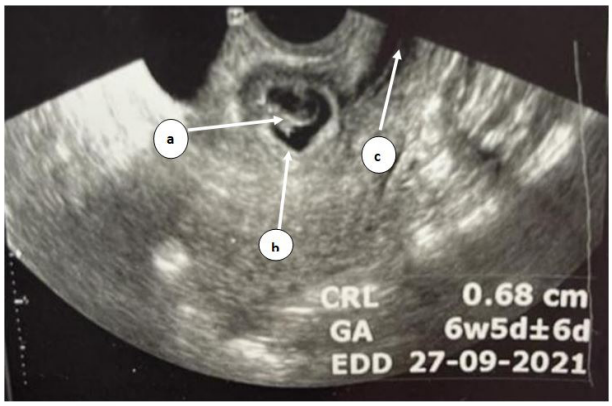

Figure 1: Transvaginal ultrasound scanning (TV/US) showing: an embryo with a Crown-Rump Length (CRL) of 68 mm; corresponding to the gestational age of 6 weeks and 5 days (a), a gestational sac implanted at the site of the previous Cesarean section scar with a live embryo (b) and an empty uterine cavity (c).

Conclusion

Operative intervention as D&C to treat CSP after failed local MTX treatment is considered as a viable option characterized by technical simplicity efficacy and avoidable or controllable intraoperative complications. This is particularly justifiable if other advanced therapeutic techniques are not available**.**

Discussion & mini-review

The presented case demonstrated a CSP which was initially managed with local injection of KCL and MTX which failed to induce a therapeutic response. Hence, *dilatation*, *evacuation* and *Curettage* (D&C) under ultrasound guidance was performed.

The possible risk factors for a CSP in our patient included one previous SC and repeated uterine curettage [7,8]. Regarding the number of previous CS or the time interval between the occurrence of a CSP and the previous section, no definitive data are yet conclusive. For example, in one study 72% of patients of CSP had two or more Cesarean deliveries [8]. On the other hand, a previous study found no clear correlation between the risk of CSP and the number of previous CS as most CSP occur after one previous CS [10]. Unexpectedly, two recent studies showed that the risk of Cesarean scar pregnancy appeared to be unrelated to the number of previous CS [11,12]. So, CSP is believed to be related to the surgical technique and possibility of a higher uterine incision due to a poorly formed lower segment [13]. Interestingly, the occurrence of CSP is reported in the absence of previous uterine surgeries, as after uterine curettage and manual separation of placenta [4], for such cases, it is suggested that CSP may occur due to endometrial trauma.

Given the potential for serious life threatening complications of the CSP, accurate and reliable diagnostic methods are required. Being an ectopic pregnancy the presentation can be variable (from minimal vaginal bleeding to severe pain, massive hemorrhage and collapse), however it's most common presentation is early pregnancy vaginal bleeding [14]. Low index of suspicion or findings misinterpretation of CSP lead to delayed diagnosis. In a recent study, the mean thickness of the Caesarean scar was only ~3 mm. and 9 cases out of 14 (~65%) showed established fetal heart activity [15]. Similarly, our patient presented with vaginal bleeding and spotting, the gestational age was 6-7 weeks (with intact fetal cardiac pulsation) and a thin layer of myometrium separating it from the bladder was seen (~2. 5 mm).

We considered Ultrasonography (US) with Doppler study as the primary diagnostic imaging technique. Combined transabdominal and transvaginal ultrasonography (TV/US) scanning with Doppler facilities, is the gold standard imaging method with a high accuracy rate in the diagnosis of a CSP [16]. Several US criteria have been developed to aid with the timely diagnosis. These criteria include an empty uterus and endocervical canal, a gestational sac at the site of the Cesarean scar, a thin or absent myometrial layer and increased blood flow between the sac and the bladder (trophoblastic circulation) with Doppler studies. The US criteria contribute to a correct diagnosis in ~86.5% of cases and to identify possible complications and/or evaluate the outcome of conservative CSP therapy. There are two recognized types of Cesarean scar pregnancies: type 1 develops in the myometrium and grows toward the uterine cavity, whereas type 2 progresses exophytically toward the uterine serosa [4,13,17].

Magnetic Resonance Imaging (MRI) is a valuable adjunct in evaluation of suspected CSP. Generally, the MRI is equally accurate with US regarding the diagnosis of CSP, but is more informative in the evaluation of scar implantation. Because of improved differentiation of soft tissue structures and spatial resolution, MRI clearly shows the gestational sac in the anterior lower uterine segment and it can assess the possibility of myometrial invasion and bladder involvement [18]. MRI can be particularly used as an adjunct to US scanning to confirm the diagnosis when the US findings are inconclusive [13,19,20].

Because of its rarity, currently, there is no consensus on the preferred mode of treatment or follow up of CSP. Various treatment modalities have been used so far, with different reported success rates [21]. In general, most of the women were treated with combined approaches [22]. A large retrospective analysis of 2037 CSP cases identified as many as 14 therapy models [23], including but not limited to expectant management, systemic or local administration of MTX, D&C, local resection of the ectopic gestational mass by minimally invasive surgery (hysteroscopy, laparoscopy), uterine artery embolization (UAE), total hysterectomy or combination of approaches. The authors' recommended approaches for treating CSP depend on availability, the severity of symptoms, and surgical skills. However, they support an interventional rather than a medical approach.

A previous systematic review [24] reported the average success rates of systemic MTX, UAE (uterine artery embolization), hysteroscopy, D&C, and hysterotomy were 8.7%, 18.3%, 39.1%, 61.6%, and 92.1%; respectively. The hysterectomy rates were 3.6%, 1.1%, 0.0%, 7.3%, and 1.7% in CSP cases that were treated by systemic MTX, UAE, hysteroscopy, D&C, and hysterotomy; respectively. Despite a live birth rate of 57% was reported in one systematic review, 63% of women managed expectantly required hysterectomy for the management of life-threatening hemorrhage following spontaneous uterine rupture or abnormally adherent placenta [25]. The high morbidity and risk of death do not justify expectant management of a viable CSP.

After careful counseling of our patient she denied opting for an interventional approach as a first choice. However, the use of systemic MTX alone *would* not be as successful option due to high levels of serum β -hCG (>87,000 mIU/ml.) Actually, a previous extensive review of the literatures concluded that ‘‘administration of primary systemic MTX treatment was found to be ideal for a CSP presenting before 8 weeks gestation, with a serum β -hCG concentration of <12,000 mIU/ml together with an absent embryonic cardiac activity [26]. Based on this mentioned recommendation, local medical treatment with MTX was performed by direct injection into the sac under ultrasound guidance. But as with the systemic intramuscular rout, the trophoblast may persist in situ and cause hemorrhage [**21**]. We used local injection of potassium chloride (KCL) to hasten embryo’s demise.

Interestingly, a previous randomized trial compared the effectiveness of local and systemic MTX in cases of CSP and found comparable success rates [27]. Moreover, another study on local administration of MTX for the treatment of CSP reported a success rate of more than 60%, however almost one out of five patients eventually required surgical management [28].

In agreement with our opinion, Shen et al. had shown that ultrasound-guided MTX injection directly into the gestational sac was associated with the least maternal morbidity. When combined with an intramuscular injection of MTX, the compli-

cation rate was less than 10%. One problem was that many care providers did not realize that MTX treatment results in a temporary increase in HCG levels, leading them to use unnecessary secondary interventions that led to serious complications [29].

To date, unfournately, there is no standard protocol for the use of MTX in CSP. There is no consensus on the dosage, number of doses needed, interval between doses or knowledge about risk factors or predictors of favorable response. Even, there was no correlation between the serum β-hCG initial levels and the favorable response to MTX, suggesting that systemic MTX could be used in CSP with higher levels of serum β-hCG [30].

During the follow-ups of our patient, after the initial local MTX injection, we were not satisfied with such a poor drop of the serum β-hCG (<15% as per the ACOG guidelines) [9]. Finally, a decision was taken to perform a *dilatation*, *evacuation* and *curettage* (D&C) under ultrasound guidance. During the procedure the whole sac was removed without any complication, and two weeks later her serum β-hCG was negative.

As regard the role of D&C in treatment of CSP, the current evidences are not yet conclusive and even conflicting. According to the previous studies and systematic reviews, D&C was the most common treatment used for CSP [31], but it was associated with high rate complications (62%). The use of curettage in the management of CSP is rather controversial, and the argument is that the procedure may lead to heavy if not catastrophic bleeding [13,23,32,33]. This is due to the massively increased vascularity associated with CSP growth in addition to the fact that the contractility of the lower segment is being poor, once hemorrhage commences it may be impossible to control it without some form of operative intervention [34].

On the other hand, some studies support a successful role for the Dilation and curettage (D&C) or Dilatation and suction curettage (D&S) in treatment of the CSP. Curettage after medical treatment showed a high rate of success and no significant effects on the intra-operative bleeding [35]. The predictors of the risk of bleeding during the procedure are gestational age and the size of gestational sac. Such a combination of MTX and curettage proposed by Ma et al. is supported by others. For instance, Wang et al. analyzed the MTX with and without curettage and showed that both therapies could treat the majority of CSP patients successfully, but the combined therapy resulted in a shorter time of therapy and had a more favorable effect [36]. Another study included 45 patients showed that MTX administration followed by suction curettage with Foley tamponade was an effective treatment for CSP [37].

In their series Giampaolino et al., [22] nineteen women (42.2%) within <8 weeks gestational age, myometrial thickness > 2 mm, and rich vascular pattern were treated with intramuscular injection of 50mg MTX and, after 48 hours then "suction curettage" under ultrasound guidance. No postoperative complications were observed at the 1-week and 1-month follow-up. This is probably due to the patient selection mode and limiting this treatment to women with earlier gestational periods eligible for the use of MTX. Again, Pristavu et al. [30] showed that, D&C is a reliable management option in management of CSP if used after inhibition of trophoblast growth and the consequent bleeding after the removal of products of conception is promptly prevented with pressure tamponade. They also found that using Mifepristone in live pregnancies is useful to hasten embryo's demise.

Recently, an updated consultant guideline, by the Society for Maternal-Fetal Medicine (SMFM), (issued in 2020) [38], included the following first authoritative recommendations on the management of CSP:

- The SMFM recommends against expectant management of Cesarean scar pregnancy (GRADE 1B);
- The SMFM suggests operative resection (with transvaginal or laparoscopic approaches when possible) or ultrasound-guided vacuum aspiration be considered for surgical management of CSP and that sharp curettage alone be avoided (GRADE 2C);
- The SMFM suggests intra-gestational MTX for medical treatment of Cesarean scar pregnancy, with or without other treatment modalities (GRADE 2C);
- The SMFM recommends that systemic MTX alone not be used to treat CSP (GRADE 1C);
- In women who choose expectant management and continuation of a CSP, the SMFM commends repeat Cesarean delivery between 34 0/7 and 35 6/7 weeks of gestation (GRADE 1C);
- The SMFM recommends that women with a CSP be advised of the risks of another pregnancy and counseled regarding effective contraceptive methods, including long-acting reversible contraception and permanent contraception (GRADE 1C).

The American College of Obstetricians and Gynecologists (ACOG), the American Institute of Ultrasound in Medicine (AIUM), and the Society of Family Planning (SFP) endorse this document [38].

In conclusion, the current literature review supports a successful role for the D&C to treat CSP after failed local MTX treatment. The first authoritative recommendations on the management of CSP issued by the SMFM and endorsed by many authorities is a step to standardize the management of CSP.

Declarations

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