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CASE SERIES

Suction Evacuation with Methotrexate as a Successful Treatment Modality for Caesarean Scar Pregnancies

Case series

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الشفط مع استخدام ميثوتريكسيت كطريقة علاج ناجحة للحمل في الندبة القيصرية

سلسلة حالات

سوميتا داتا و شيترا جه

ABSTRACT: Pregnancy resulting from the implantation of an embryo within a scar of a previous Caesarean section is extremely rare. The diagnosis and treatment of Caesarean scar pregnancies (CSPs) are challenging and the optimal course of treatment is still to be determined. We report a case series of six patients with CSPs who presented to the Royal Hospital in Muscat, Oman, between October 2012 and April 2014. All of the patients were successfully treated with systemic methotrexate and five patients underwent suction evacuation either before or after the methotrexate administration. The patients were followed up for a period of 6–9 weeks after treatment and recovered completely without any significant complications. Suction evacuation with methotrexate can therefore be considered an effective treatment option with good maternal outcomes.

Keywords: Ectopic Pregnancy; Caesarean Section; Scar; Suction Curettage; Methotrexate; Case Series; Oman.

الملخص: الحمل الناتج عن غرس الجنين داخل ندبة لعملية قيصرية سابقة حالة نادرة للغاية. تشخيص وعلاج حالات الحمل في الندبة القيصرية صعبة والسبيل الأمثل للعلاج لم يتعين بعد. نعرض هنا سلسلة حالات لستة نساء يعانون من الحمل في الندبة القيصرية قدمن إلى المستشفى الملكي في مسقط، عمان، بين أكتوبر 2012 وأبريل 2014. تم علاج جميع المريضات بنجاح باستخدام الميثوتريكسيت العام وخضعت خمسة من المريضات للشفط الهوائي سواء قبل أو بعد العلاج بالميثوتريكسيت. تمت متابعة المريضات لمدة 6–9 أسابيع بعد العلاج والشفاء التام دون أي مضاعفات خطيرة. وبالتالي، يمكن اعتبار الشفط الهوائي مع الميثوتريكسيت خيار علاجي فعال مع نتائج جيدة.

مفتاح الكلمات: الحمل خارج الرحم؛ عمليه قيصرية؛ ندبة؛ شفط كحت؛ الميثوتريكسيت؛ سلسلة حالات؛ عمان.

Caesarean scar pregnancy (CSP) is a rare and potentially dangerous type of ectopic pregnancy resulting from the implantation of an embryo within the area of a previous Caesarean section scar.[1] It is a complication which can be attributed to the recent worldwide increase in Caesarean births.[2] The early and accurate diagnosis of such cases is essential, as a CSP can be easily confused with an undetected/silent miscarriage, an incomplete miscarriage during the expulsion process or a cervical ectopic pregnancy.[3]

Due to the lack of reported data regarding CSPs, the true incidence of this complication is difficult to determine; studies have reported an incidence of one in 1,800 to one in 2,216 pregnancies.[4–6] CSP has been found to represent 6.1% of all ectopic pregnancies where there is a history of at least one Caesarean section.[6] CSP was first reported in the English medical literature in 1978.[7] Only 19 cases were reported between 1966 and 2002; however, this number rose to 268 in the following eight years.[1,8] The increase in reported CSP cases may have been influenced by the rise of Caesarean sections, along with the more widespread availability and well-defined criteria of the transvaginal scan which aids in the earlier detection of such pregnancies. Notwithstanding this recent development, current knowledge regarding the management of this potentially life-threatening condition continues to be based mainly on individual case reports and a small number of case series. Suction evacuation or primary curettage are often reported as the least favoured treatment options due to their associated complications.[9,10]

This case series presents six patients with CSPs

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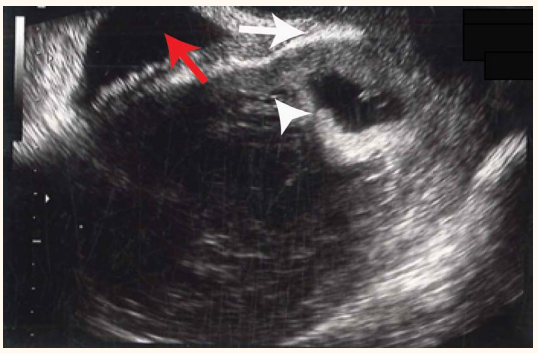

Figure 1: Vaginal ultrasound showing a pregnancy in the Caesarean scar site (white arrow) growing towards the endometrial cavity (arrowhead). The bladder can also be observed (red arrow).

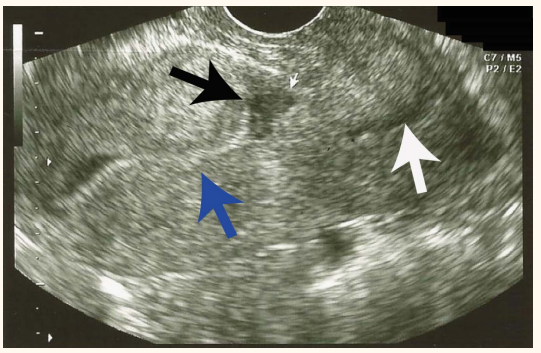

Figure 2: Vaginal ultrasound of an empty endometrial cavity (blue arrow) and cervix (white arrow) with a pregnancy at the Caesarean scar site (black arrow).

treated successfully with a combination of systemic methotrexate and suction evacuation at the Royal Hospital in Muscat, Oman, between October 2012 and April 2014. All patients consented to the publication of their anonymised data.

Case 1

A 33-year–old woman was referred to the Royal Hospital in October 2012 at seven gestational weeks into her seventh pregnancy. She had had one lower segment Caesarean section five years previously, followed by a vaginal birth. At presentation, the patient had a three-day history of vaginal bleeding with clots and her β-human chorionic gonadotropin (β-hCG) level was 9,400 IU/L. A CSP was suspected [Figure 1] and she was referred to the Royal Hospital after receiving one intramuscular dose of 80 mg/m^2 of methotrexate the previous day. After undergoing counselling regarding her available treatment options—repeated administration of methotrexate or surgical evacuation—the patient opted for the latter modality. During the procedure, the patient lost 200 mL of blood and a Foley catheter was inserted into the uterine cavity. The patient had an uneventful postoperative course; her β-hCG level dropped to 3,336 IU/L after four days and she was discharged and followed up as an outpatient. After eight weeks, the patient's β-hCG level was negative. The small haematoma in the scar site resolved after 12 weeks.

Case 2

A 30-year-old woman presented to Royal Hospital in November 2013 at five gestational weeks into her third pregnancy with abdominal pain and mild vaginal bleeding. She had had two lower segment Caesarean sections in the past and a laparoscopic left ovarian cystectomy for a dermoid cyst 11 days previously. At presentation, her β-hCG level was 4,980 IU/L; however, this rose to 10,907 IU/L after 48 hours. An ultrasound scan suggested a CSP and this was later confirmed by magnetic resonance imaging (MRI). The patient received one dose of 50 mg/m^2 of methotrexate when her β-hCG level reached 38,452 IU/L. She underwent a suction evacuation two days later during which she lost 700 mL of blood. The postoperative course was uneventful; her β-hCG level dropped to 3,867 IU/L after four days and she was discharged and followed up as an outpatient. Her β-hCG level was negative after eight weeks. The patient had an intrauterine pregnancy the following year which unfortunately resulted in early fetal death. She subsequently underwent another successful suction evacuation.

Case 3

A 35-year-old woman presented to the Royal Hospital in October 2013 at 11 gestational weeks into her fifth pregnancy with mild vaginal bleeding and pain. She had had a lower segment Caesarean section four years previously due to grade 3 anterior placenta *praevia* partially covering the internal opening of the cervix. A transvaginal scan showed a collapsed intrauterine gestational sac in the lower uterine segment with fetal pole and no fetal cardiac activity [Figure 2]. The patient's β-hCG level was 12,971 IU/L. A diagnosis of a silent miscarriage was made and she received two doses of 800 µg of misoprostol. The patient underwent a suction evacuation two days later as she did not respond to the treatment. Although the patient lost 500 mL of blood during the procedure and her haemoglobin dropped by 2 g%, she did not require a blood transfusion.

The patient was discharged two days after the surgery but was readmitted 10 days later with heavy

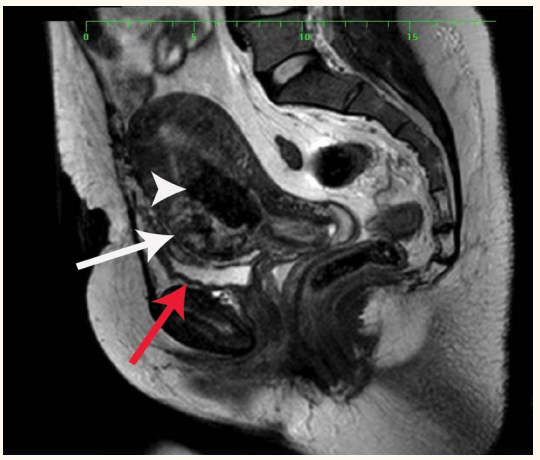

Figure 3: Magnetic resonance image of the pelvis showing a Caesarean scar pregnancy (white arrow) with an empty but dilated endometrial cavity (arrowhead). The bladder can also be observed (red arrow).

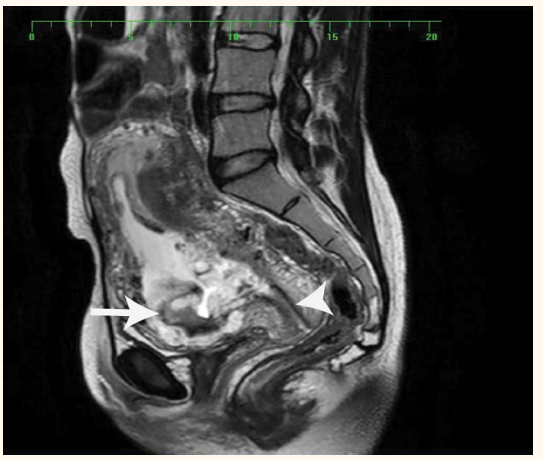

Figure 4: Magnetic resonance image of the pelvis showing a scar pregnancy (white arrow) with an empty endometrial canal and cervix (arrowhead).

bleeding. A CSP was suspected following an ultrasound and confirmed by MRI; a morbidly adherent placenta and haematoma formation in the anterior wall was also observed. Her β-hCG level was 1,741 IU/L and she was given one dose of 50 mg/m^2 of methotrexate. She was followed up as an outpatient. Her β-hCG level was negative after 10 weeks; however, the haematoma persisted for four months. The patient was advised to undergo an early elective lower segment Caesarean section at 37–38 gestational weeks during her next pregnancy.

Case 4

A 40-year-old woman was referred to the Royal Hospital in December 2013 at 16 gestational weeks into her sixth pregnancy with a diagnosis of a silent miscarriage. She had had three previous Caesarean sections, the last one occurring during the previous year. She received three doses of 800 µg of misoprostol and then opted for surgical evacuation. She bled 2,500 mL during the evacuation and required tamponade by a Foley catheter in the uterine cavity. The patient received two units of blood with six units of fresh frozen plasma. The uterine Foley catheter was removed after 24 hours and the patient was subsequently discharged.

The patient was readmitted one week later with heavy vaginal bleeding. A CSP was suspected and then confirmed by MRI [Figure 3]. Her β-hCG level was 15 IU/L and she was given one dose of 50 mg/m^2 of methotrexate. After four weeks, during a subsequent outpatient follow-up appointment, it was noted that her β-hCG level had returned to negative and the residual pregnancy mass in the anterior uterine wall had resolved.

Case 5

A 32-year-old woman with a history of three lower segment Caesarean sections was referred to the Royal Hospital in March 2014 at nine gestational weeks into her fourth pregnancy. She was referred due to a suspected silent miscarriage and molar pregnancy. She underwent a transvaginal scan which raised the suspicion of a CSP; this was later confirmed by MRI [Figure 4]. Her β-hCG level was 25,261 IU/L and she received one dose of 50 mg/m^2 of methotrexate.

At a follow-up appointment one week later, her β-hCG level was 5,389 IU/L and she received a second dose of 50 mg/m^2 of methotrexate. She then developed vaginal bleeding and underwent an emergency evacuation of the uterus, during which she lost 1,000 mL of blood. An intrauterine Foley catheter was inserted and uterine artery embolisation (UAE) was performed. Four days after surgery, her β-hCG level decreased significantly to 1,049 IU/L; it became negative after five weeks and the patient recovered well.

Case 6

A 39-year-old woman was referred to the Royal Hospital in April 2014 at 11 gestational weeks into her fifth pregnancy with a suspected silent miscarriage. She had a history of four previous lower segment Caesarean sections. She received three 800 µg doses of misoprostol but failed to respond to the treatment. A CSP was suspected and was confirmed by transvaginal scan. A combined transvaginal and transabdominal scan of the patient with a full bladder was performed. The patient received one dose of 50 mg/m^2 of methotrexate. The subsequent follow-up period showed a decline in her β-hCG level to <1 IU/L

Table 1: Clinical, radiological and interventional characteristics of each of the six presented patients with Caesarean scar pregnancies

Age in years	Obstetric history	Years since last LSCS	Symptoms	Gestational weeks + days	β-hCG in IU/L	Imaging modality	Treatment	Follow-up period in weeks	Blood loss
33	•G 7, P 6 •Four previous births via SVD •One previous birth via LSCS •One previous birth via VBAC	5.0	Vaginal bleeding	7 + 0	9,400	•TV scan	•Methotrexate •Evacuation	9	•Minimal
30	•G 3, P 2 •Two previous births via LSCS •Laparoscopic cystectomy performed 11 days before presentation	1.5	Abdominal pain and mild vaginal bleeding	4 + 5	38,452	•TV scan •MRI	•Methotrexate •Evacuation	8	•700 mL •One unit of blood transfused
35	•G 5, P 4 •One previous birth via LSCS due to grade 3 anterior placenta *praevia*	4.0	Heavy bleeding after evacuation for suspected silent miscarriage	11 + 4	1,741	•TV scan •MRI	•Evacuation •Methotrexate	8	•500 mL
40	•G 7, P 6 •Three previous births via LSCS	1.5	Heavy bleeding after evacuation for suspected silent miscarriage	16 + 0	15	•TV scan •MRI	•Evacuation •Methotrexate	6	•2,500 mL •Two units of blood transfused •Six units of FFP transfused
32	•G 4, P 3 •Three previous births via LSCS	2.5	Asymptomatic	9 + 2	25,261	•TV scan •MRI	•Methotrexate (two doses) •Evacuation •UAE	7	•1,000 mL •One unit of blood transfused
39	•G 5, P 4 •Four previous births via LSCS	5.0	Asymptomatic	11 + 3	1,013	•TV scan •TV/TA scan	•Methotrexate	8	•Minimal

LSCS = lower segment Caesarean section; β-hCG = β-human chorionic gonadotropin; G = gravida; P = para; TV = transvaginal; SVD = spontaneous vaginal delivery; VBAC = vaginal birth after Caesarean section; MRI = magnetic resonance imaging; FFP = fresh frozen plasma; UAE = uterine artery embolisation; TA = transabdominal.

after five weeks. The pregnancy mass had resolved after four weeks.

Clinical and treatment details for each patient are presented in Table 1. Overall findings for the case series are presented in Table 2. Histopathology results for all patients showed products of conception. Outpatient follow-up included weekly checks of serum β-hCG levels until the values had returned to normal. Weekly ultrasound scans were performed until the CSP had resolved completely. All of the women recovered completely with no methotrexate-related side-effects and no additional medical or surgical interventions. Those who were planning further pregnancies were advised regarding the optimal timeframe for their next pregnancy and were encouraged to have early vaginal scans during their next pregnancy to confirm the intrauterine location of the embryo.

Discussion

There has been a rise in the reported incidence of CSP in the medical literature in recent years.[2] Although a series of 18 and eight CSP cases were reported by Jurkovic *et al*. and Maymon *et al*., respectively, the majority of data on CSP are found in individual case reports or small case series.[4,11] To the best of the authors' knowledge, this is the first case series to exclusively present suction evacuation and methotrexate as a treatment modality; this will hopefully aid in the acceptance of this approach as an effective treatment option for CSP.

Vial *et al*. proposed two different types of CSP; the first occurs due to the implantation of the gestational sac on the scar with progression towards either the cervico-isthmic space or uterine cavity and the second as a result of a deep implantation into a post-Caesarean section defect with growth towards the bladder.[12]

Table 2: Summary of the clinical characteristics, imaging modality, interventions and recovery of the six presented patients with Caesarean scar pregnancies

	n (%)
Characteristics	
Mean maternal age in years (range)	35 (30–40)
Gravidity (range)	5 (3–7)
Mean gestational age at diagnosis in weeks (range)	11 (5–16)
Spontaneous conception	6 (100.0)
History of LSCS	5 (83.3)
Imaging modality	
Transvaginal ultrasonography	6 (100.0)
Transabdominal ultrasonography	1 (16.7)
Magnetic resonance imaging	4 (66.7)
Interventions	
Blood transfusion	3 (50.0)
•One unit	2 (33.4)
•Two units	1 (16.7)
Systemic methotrexate	6 (100.0)
•First-line followed by suction evacuation	3 (50.0)
•First-line with no subsequent intervention required	1 (16.7)
•Following evacuation	2 (33.4)*
Suction evacuation	5 (83.3)
UAE following suction evaluation	1 (16.7)
Recovery	
Mean follow-up in weeks (range)	8 (6–9)
Full recovery	6 (100.0)
Methotrexate-related side-effects	0 (0.0)
Additional interventions	0 (0.0)

LSC = lower segment Caesarean section; UAE = uterine artery embolisation.

**These two patients underwent a suction evacuation for a missed/silent miscarriage before the correct diagnosis of CSP was made at readmission.*

While the first type of pregnancy may result in a viable birth, it has an increased risk of life-threatening bleeding from the implantation site.[7,13] The second generally leads to a rupture and bleeding during the first trimester.[12]

The clinical presentation of patients in the current case series reflects the wide range of symptoms associated with this rare kind of ectopic pregnancy. Symptoms varied from slight vaginal bleeding and pain to profuse vaginal bleeding and, ultimately, silent miscarriages. These cases therefore highlight the potential difficulties in achieving an accurate diagnosis at presentation. Early diagnosis is paramount in CSP to increase the number of available treatment options and to avoid serious complications like haemorrhage and uterine rupture. Many undiagnosed CSP patients present with heavy bleeding, shock and haemoperitoneum after the termination of an early pregnancy or dilatation following a silent miscarriage, as was the case in two of the patients in the current series.

Transvaginal ultrasonography has been reported as a first-line diagnostic tool, with a sensitivity rate of 86.4%.[5] Sonographic criteria for diagnosing CSP include an empty uterus without contact with the gestational sac; a visibly empty cervical canal; the presence of the gestational sac with or without a fetal pole and with or without fetal cardiac activity (depending on the gestational age) in the anterior segment of the uterine *isthmus*; and the absence of or a defect in the myometrial tissue between the bladder and the gestational sac.[1,7] All cases of CSP in the current series fulfilled these criteria. With transvaginal ultrasonography, a diagnosis of CSP can be confidentially made using a sagittal view along the long axis of the uterus through the gestational sac.[7] Maymon *et al*. recommended a dual approach, combining transvaginal and transabdominal scans of the patient with a full bladder; the latter provides a 'panoramic' view of the uterus and an accurate measurement of the distance between the gestational sac and the bladder.[11] This technique was used to diagnose CSP in one patient in the current case series, as the patient's uterus was pulled up due to her four previous Caesarean surgeries. Another diagnostic method proposed by Jurkovic *et al*. is the negative sliding organ sign, defined as the inability to displace the gestational sac from its position at the level of the internal cervical opening using gentle pressure applied with a transabdominal probe.[4]

As yet, there is no proven relationship between the number of previous Caesarean sections, or the time interval between Caesarean sections, and the subsequent development of CSP. Jurkovic *et al*. found that 72.0% of their patients had previously had two or more Caesarean sections;[4] a similar percentage was observed in the current case series, with 66.7% of the patients having previously had two or more Caesarean sections. Previous Caesarean section scars should be examined routinely during early pregnancy to help reduce the misdiagnosis of CSPs as silent miscarriages and to improve maternal morbidity and mortality.

In the absence of a standard treatment protocol for CSP, a number of treatment options exist, either singly or in combination, with varied success rates. Important factors influencing choice of treatment

include the clinical stability of the patient, gestational age, size of the ectopic pregnancy mass, β-hCG levels and any known contraindication to methotrexate therapy. All treatment regimens aim to resolve the CSP prior to rupture and preserve future fertility, if desired. In the literature, almost all of the women whose pregnancies were managed expectantly developed placenta *accreta* or *increta*, resulting in either a hysterotomy or hysterectomy with severe haemorrhage.[7] The pathophysiology of scar implantation has been suggested as a precursor of placenta *accreta*.[14] Therefore, most diagnosed cases are treated by either surgical or medical means or a combination of both. Suggested medical treatments involve the administration of local intragestational methotrexate; systemic methotrexate; potassium chloride; hyperosmolar glucose; or a combined approach with varying regimens.[15–17]

Fadhlaoui *et al.* reported the combination of medical modalities, either systemic or local and as a single agent or a combined regimen, with aspiration of the gestational sac.[18] This approach can preserve fertility and avoid an unnecessary laparotomy; however, it requires close monitoring and follow-up of the patient as the normalisation of β-hCG levels may take up to 4–16 weeks.[15,16,19] In their analysis of published case reports, Jurkovic et al. found that medical treatment with methotrexate was successful in 71.0–80.0% of cases, with 6.0% of women requiring a hysterectomy.[4]

To date, 17 cases of CSP involving uterine curettage as the primary therapy have been reported in the medical literature.[9,10,20] Arslan *et al.* reported unsuccessful or complicated uterine curettage in eight out of nine women,[9] whereas Wang *et al.* reported a failure rate of 70.0% after curettage.[20] This could be attributed to an inability to evacuate all of the ectopic tissue and the increased risk of uterine rupture and severe haemorrhage.[20] However, some reports have suggested that dilatation and curettage should be considered in cases with early presentation (<7 gestational weeks) and in those with sufficient myometrial tissue between the gestational sac and the bladder (>3.5 mm).[9,18,20] Additional adjunct and haemostatic measures—such as vasopressin, intrauterine balloon tamponade with a Foley catheter, bilateral UAE and bilateral uterine artery ligation—have been used for the prevention and control of profuse bleeding in a variety of treatment settings.[4,21–23]

Minimally invasive treatment modalities are usually determined by the type of CSP, with a laparoscopic approach being suitable for deeply implanted pregnancies growing towards the abdominal cavity, while a hysteroscopic approach may be considered in those growing towards the uterine cavity. Hysteroscopic evacuations have been reported by Wang *et al.* and Chao *et al.* after failed curettage and methotrexate treatment.[24,25] Laparoscopic removal of the CSP and laparoscopically-assisted operative hysteroscopy have also been reported as treatment options in cases where the patient is stable and appropriate facilities with a trained surgeon are available.[26,27] Surgical treatment, either a laparotomy with wedge resection or a hysterectomy, should be considered in haemodynamically unstable patients with late presentation of the CSP, those presenting with uterine rupture, in the event of failed medical/surgical treatment or for cases where operative endoscopy is not feasible. A laparotomy has the advantage of completely removing the CSP mass and repairing the scar at the same time, followed by the normalisation of β-hCG levels within 1–2 weeks.[1,11]

Long-term complications following treatment of a CSP include fertility issues and recurrence. A follow-up study of 29 women who were successfully treated for CSP reported favourable reproductive outcomes and a low recurrence rate.[28] Out of 24 women attempting to become pregnant, 21 conceived spontaneously (20 intrauterine pregnancies and one recurrent CSP); of the intrauterine pregnancies, 13 were normal (nine of which were delivered by Caesarean section) while seven ended in spontaneous miscarriages.[28] Using sonohysterography, the integrity of the uterine wall post-Caesarean section can be determined even in non-pregnant patients.[2,29] Caesarean scar defects, defined by the presence of fluid within the incision site, or any filling defects at the presumed scar site might indicate uterine scar complications in a subsequent pregnancy.[4,29] Counselling and treatment options for these patients should therefore be tailored accordingly.

Conclusion

CSP is a potentially life-threatening complication following a previous Caesarean birth and an exponential rise in the incidence of this type of pregnancy has recently been recorded. Bleeding and pain in early pregnancy are the most common presenting symptoms. Examining the appearance of a previous Caesarean section scar should be a routine procedure in every early pregnancy to help reduce misdiagnosis and maternal morbidity and mortality. There is no general consensus on the most effective treatment modality for CSP; however, this case series shows that suction evacuation combined with methotrexate is a successful treatment option with good maternal outcome.

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