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Cesarean Scar Pregnancy: A Tertiary Care Center Experience

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Abstract

Objectives: To describe the management and treatment outcomes of cesarean scar pregnancies diagnosed in a tertiary care center.

Methods: This study retrospectively described all cases of cesarean scar pregnancy diagnosed and managed at a tertiary care center over a 3-year period. Maternal demographics, clinical presentation, treatment methods, and outcomes were all included in the analysis.

Results: uring the study period, 5 cases of cesarean scar pregnancy were diagnosed and managed. The median gestational age at diagnosis was 8 weeks, and all fetuses had positive cardiac activity. All cases were initially treated with systemic intramuscular (IM) methotrexate (MTX), but only one case responded well due to fetal bradycardia present prior to treatment. One patient received further management with transvaginal intracardiac potassium chloride (KCL) injection, which resulted in maternal sepsis, hemorrhage, and ICU admission. The other 3 cases were managed by transabdominal intra-gestational sac MTX +/- KCL and showed good clinical response. Two of these cases required an interval dilation & curettage (D&C) due to persistent vaginal spotting with no complications.

Conclusions: It is recommended to avoid using systemic IM MTX as the first-line treatment for scar pregnancy unless the pregnancy is failing or non-viable. Intra-gestational sac treatment may cause persistent retained products of conception, leading to bothersome vaginal spotting. An interval ultrasound guided D&C appears to be safe for managing this complication, but the exact interval needs to be determined through further studies. Sepsis is a rare complication of invasive medical treatment, and close surveillance is advised.

Keywords: Scar ectopic, cesarean, Methotrexate, Case series, Intra-gestational injection

Introduction

Cesarean scar pregnancy (CSP) occurs when the early pregnancy is implanted in the defect of an earlier cesarean section and can be associated with severe maternal morbidity (1). Its incidence is reported to be around 1:1800 pregnancies (2). Two varieties of CSP have been illustrated: type 1 (endogenic type) occurs when the pregnancy develops towards the uterine cavity, and type 2 (exogenic type) takes place when the pregnancy substantially advances the scar defect and grows towards the bladder and the abdominal cavity (3). Unlike tubal pregnancies where a clear protocol and well-established criteria for management are present, there is no agreement on how to achieve the optimal management of cesarean scar pregnancies. Also, there is no clear distinction in the management of the two different types of scar pregnancies. The management options in general include expectant management, systemic methotrexate (MTX), intra-gestational sac MTX, operative resection, and ultrasound-guided vacuum aspiration (1). The objective of our investigation was to discuss the methods used and clinical outcomes of cesarean scar pregnancies examined and managed in our maternal-fetal medicine department.

Methods

This was a retrospective descriptive study of all women diagnosed with CSP at King Abdulaziz University Hospital, from January 2018 till December 2020. The medical record numbers were obtained from the Maternal Fetal Medicine Department where all cases were scanned and the diagnosis of CSP was confirmed. By following Ash and colleagues' guidelines (4), the diagnosis was established; the presence of one or more of the following confirmed the diagnosis of CSP: 1) the uterine cavity is empty and is not in touch with the gestational sac, 2) the cervical canal is empty and does not come into contact with the gestational sac, 3) the anterior lower region of the uterine segment contains the gestational sac, and 4) there is a myometrial deficiency or lack of the myometrium between the bladder and the gestational sac.

Moreover, the following variables were recorded by 2 investigators from the patient's electronic medical files including mother's age, gravidity, parity, abortions, number of prior cesarean surgeries, level of initial beta-human chorionic gonadotropin (β-hCG), gestational at diagnosis, the existence of fetal cardiac activity, time to negative β-hCG, presenting symptoms, treatment modality, and

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Key Messages

- The use of intra-gestational sac MTX has been found to be effective in managing cesarean scar pregnancy. However, it may be associated with bothersome vaginal spotting. In cases where this is a concern, an interval dilation and curettage procedure can be considered as a safe alternative.

complications. To maintain patient confidentiality, the information was stored on a private computer with access granted solely to the principal investigator.

Results

Between January 2018 and December 2020, 5 cases of CSP were diagnosed. All the cases were referred from other healthcare facilities and the diagnosis was confirmed in our fetal medicine department. Table 1 summarizes all 5 cases.

With a median gravidity of 5 (range 4-6) and a median parity of 3 (range 2-5), the mean maternal age upon diagnosis was 36.2 years. The average number of preceding cesarean sections was 3. The clinical presentation was vaginal bleeding in 2 cases and incidental ultrasound findings in the remaining 3. At diagnosis, the average gestational age was 8 weeks +/- 1 week, all fetuses had positive cardiac activity and were type 1 CSP. The mean β-hCG at diagnosis was 134 422 IU/L. All patients initially obtained systemic intramuscular (IM) MTX. One case received multi-dose therapy, consisting of 1 mg/kg MTX on days 1, 3, 5, and 7, and 0.1 mg/kg of folinic acid on days 2, 4, 6, and 8, administered intramuscularly. Three cases received a single dose of MTX (50 mg/m^2), while one case received two doses. One case received transvaginal intracardiac fetal potassium chloride (KCL) injection (2 mL of 2 mEq/mL), and three cases received transabdominal intra-gestational sac MTX (50 mg/m^2) and KCL (1.5-2 mL of 2 mEq/mL) injection. Dilation and curettage (D&C) was required in four cases, with one being an emergency due to active bleeding, and the other three due to persistent spotting from retained products of conception (RPOC). A brief description of each case is presented in the study.

Case 1

A 33-year-old woman, Gravida 4, Para 2, Abortion 1, with a history of two cesarean sections, presented at nine weeks gestation with mild vaginal bleeding. Transvaginal ultrasound revealed a scar ectopic pregnancy (Figure 1), with an initial β-hCG level of 60 557 IU/L. She received a single systemic dose of MTX, but two days later, persistent fetal cardiac activity was observed. Transvaginal fetal intracardiac KCL injection was administered, and fetal demise was confirmed. Four days later, she presented to the emergency room with fever and epigastric pain. She was hypotensive with a blood pressure of 91/60, and lab results showed a β-hCG of 31,127 IU/L, leukopenia (WBC 0.85), and neutropenia (neutrophils 0.53), with normal hemoglobin and platelet counts. Blood cultures were obtained, and she was started on empiric antibiotics. She experienced heavy vaginal bleeding and underwent an emergency D&C; products of conception were sent for pathology. Her estimated blood loss was one liter, and she received two units of packed red blood cells and four liters of crystalloids in the operating room. In recovery, she became hypoxic and developed acute pulmonary edema, requiring reintubation and transfer to the ICU for

Table 1. Clinical Characteristics and Management Outcomes of Scar Ectopic

	Case 1	Case 2	Case 3	Case 4	Case 5
Maternal age (y)	33	39	35	39	35
Gravidity	4	5	5	4	6
Parity	2	4	3	3	5
Abortions	1	0	1	0	0
Number of C/S	2	3	3	3	2
Presenting symptom	Vaginal bleeding	Incidental US	Vaginal bleeding	Incidental US	Incidental US
GA at Dx	9 weeks	7.3 weeks	6.7 weeks	8.4 weeks	8.7 weeks
Fetal heart	+	+	+	+	+
Presenting β-hCG	60,557	56,241	217,076	305,661	32,575
First-line treatment	Single-dose systemic MTX	2 doses of systemic MTX	Multidose systemic MTX	Single-dose systemic MTX	Single-dose systemic MTX
Second-line treatment	Transvaginal intracardiac KCL	Transabdominal Intra-gestational sac MTX	D&C	Transabdominal Intra-gestational KCL and MTX	Transabdominal Intra-gestational sac KCL and MTX
Third-line treatment	D&C	Transabdominal intra-gestational sac KCL	None	D&C	One dose systemic MTX
Fourth-line treatment	None	None	None	None	D&C
Time to -ve β-hCG	1 month	4 months	4 months	2.5 months	1.5 months
Complications	Sepsis and ICU stay	None	None	None	None

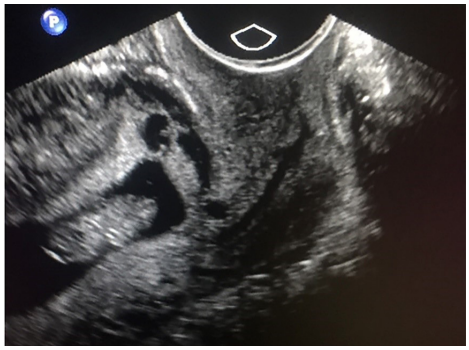

Figure 1. Implantation of the sac and placenta into the cesarean scar with placental lacunae suggesting early onset placenta accreta spectrum. A 9 weeks viable fetus was present (Case 1).

three days of mechanical ventilation. Her antibiotics were changed to meropenem and vancomycin after admission blood cultures showed *Peptostreptococcus asaccharolyticus*. She developed disseminated intravascular coagulation during her ICU stay but responded to medical treatment. On the fourth day of her ICU stay, she was extubated and transferred to the gynecology floor. Her antibiotics were switched to Tazocin for four days and then Augmentin 625 mg three times daily for two weeks as an outpatient treatment. She was discharged from the hospital in good condition four days after her transfer from the ICU and had a negative β-hCG level during her one-week outpatient follow-up.

Case 2

A 39-year-old woman, Gravida 5, Para 4, with a history of three previous cesarean sections, was incidentally diagnosed with a scar ectopic pregnancy during an ultrasound at 7 weeks+3 days. Fetal cardiac activity was positive, and her β-hCG level at admission was 56 241 IU/L. She received two doses of systemic IM MTX one week apart, but persistent fetal cardiac activity was observed on day 8. Intra-gestational sac MTX was administered, but fetal cardiac activity persisted the next day. KCL was injected into the intra-gestational sac, and cardiac arrest was confirmed. The patient was monitored using serial ultrasounds and β-hCG levels. Four months after diagnosis, the β-hCG level became negative, and a small amount of retained products measuring 8 mm were found on ultrasound. She was lost to follow-up and returned one year later with secondary infertility. Normal results were obtained from a hysterosalpingogram and pelvic ultrasound, but semen analysis revealed male factor infertility. She was advised to undergo *in vitro* fertilization but never returned for follow-up.

Case 3

A 35-year-old woman, Gravida 5, Para 3, Abortion 1, with a history of three cesarean sections presented at 6 weeks+5 days with intermittent vaginal bleeding two days after a confirmed pregnancy test. Ultrasound revealed a gestational sac implanted in the previous scar with a fetal pole measuring 7 weeks with bradycardia. MRI confirmed the diagnosis (Figure 2a, 2b), and her β-hCG level at presentation was 217,076 IU/L. Fixed multiple doses of MTX (1 mg/kg intramuscularly on days 1, 3, 5, and 7 alternating with 0.1 mg/kg of folinic acid intramuscularly on days 2, 4, 6, and 8) were administered due to impending fetal demise. Absent fetal cardiac activity was observed on day 5, and serial ultrasounds and β-hCG levels were monitored. Four months after diagnosis, the β-hCG level became negative, but retained products measuring 4.4 x 2.8 cm were found on ultrasound up to five months after treatment. The patient complained of persistent intermenstrual bleeding but deferred surgery due to social reasons. Ultrasound-guided dilation and curettage was eventually performed five months after medical treatment with minimal blood loss and no complications. Two years later, she presented at 12 weeks for a nuchal translucency scan, and a normal intrauterine pregnancy was found. She delivered with a repeat cesarean section at term in another institution without complications.

Case 4

A 39-year-old woman, Gravida 4, Para 3, with a history of three previous cesarean sections was referred from another hospital at 8 weeks+3 days with a diagnosis of scar ectopic pregnancy incidentally found by ultrasound. A single dose of IM MTX was given at that hospital. In our unit, the presence of a scar pregnancy was confirmed, and a viable fetus was discovered. Upon admission, her initial β-hCG level was 305,661 IU/L. Transabdominal intra-gestational sac MTX and KCL were administered with good clinical response as evidenced by falling β-hCG levels. The patient experienced persistent vaginal spotting and recurring abdominal cramping after 2.5 months. Ultrasound showed persistent retained products measuring 7.5 x 5 cm; hence, dilation and curettage under ultrasound guidance was performed with no complications.

Case 5

A 35-year-old woman, Gravida 6, Para 5, with a history of two previous cesarean sections was referred from another hospital as a case of scar pregnancy where she received a single dose of systemic MTX with no clinical response. The diagnosis was confirmed in our center, and a viable

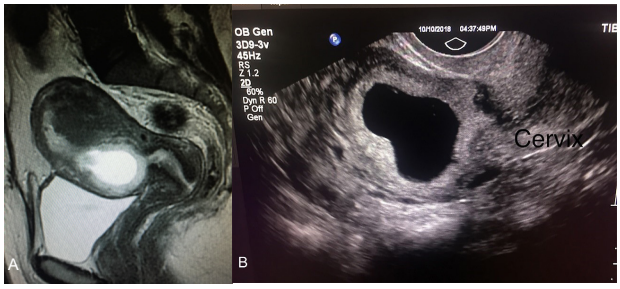

Figure 2. MRI and transvaginal ultrasound showing the low implantation of the gestational sac into the previous cesarean scar (Case 3).

fetus measuring 8 weeks+5 days was present (Figure 3). Her initial β-hCG level in our hospital was 32,575 IU/L. Intra-gestational sac KCL and MTX were administered, followed by weekly β-hCG monitoring. The drop in β-hCG levels from week 3 to 4 was less than 15%, so an additional single dose of systemic MTX was given. Two weeks later, the patient came to the clinic complaining of persistent vaginal bleeding and infrequent cramps; thus, she was scheduled for an elective D&C. One week later, under ultrasound guidance, 4 x 3 cm RPOC was discovered, and D&C was performed. A moderate amount of tissue was removed and sent to pathology. Overall, she did well with no complications.

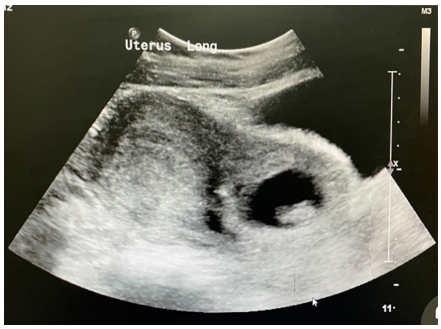

Figure 3. A transabdominal appearance of the cesarean scar pregnancy (Case 5).

Discussion

CSP is a very uncommon but growing obstetric obstacle that can cause severe maternal morbidity. The clinical presentation is variable including vaginal bleeding, abdominal pain, and an asymptomatic incidental finding on ultrasound. As opposed to Riyaz and colleagues' findings, where 90% of their cases were symptomatic, 60% of our patients were incidentally diagnosed by ultrasound, and vaginal bleeding only occurred in 40% of them (5).

For patients with previous cesarean surgery, early first-trimester universal screening has been suggested to detect the pregnancy location. In one study, earlier diagnosis (<9 weeks) was associated with less maternal bleeding, blood transfusion requirements, uterine rupture, and urgent hysterectomy (6). Timor-Tritsch et al recommend that transvaginal ultrasound to be done at 5 to 7 weeks as a component of routine antenatal care for patients with prior cesarean section to rule out CSP and placenta accrete spectrum (7). At diagnosis, the average gestational age in our study reached 8 weeks +/- 1 week which is similar to the 7.5 weeks +/- 2.5 weeks reported by Rotas et al (8). On average, the prior cesarean sections' number in our study was 3. It is controversial whether having more cesareans increases a women's risk of developing a CSP. According to Jurkovic et al, 72% of the patients involved repeated cesarean sections (2); in contrast, based on a review of 112 cases, Rotas et al found that 52% of cases occurred among females with one prior c-section (8).

Generally, all our cases received at least a single dose of systemic IM MTX, with persistent fetal cardiac activity demonstrated in all but one case, where multidose treatment was given and fetal bradycardia was detected before treatment. Notably, good clinical response with the multidose (case 3) was noted but persistent intermenstrual bleeding and retained products after 5 months of medical treatment ultimately led to performing a dilation and curettage with no complications. Two years later, she had a successful term pregnancy. A review by Timor-Tritsch et al proved that using systemic MTX as a first-line treatment in 87 cases resulted in a 62 % complication rate, defining complications as the need for a second intervention (9). Recently, the SMFM recommended against using systemic MTX alone as a primary method for pregnancies with cesarean scars due to its high complication rate (1). In very early, nonviable, or failing scar pregnancies, systemic MTX may be useful, as illustrated in our case with fetal bradycardia and positive clinical response to the MTX multidose therapy. This was also suggested by Haimov-Kochman et al (10). Furthermore, Ammar et al demonstrated a 100% success rate for systemic MTX in their nonviable scar pregnancies (11).

Transvaginal fetal intracardiac injection of KCL was done in case 1 after failed initial systemic MTX. Ammar et al demonstrated in their study including 20 live scar pregnancies that administration of intra-gestational sac or intra-cardiac KCL combined with systemic MTX accomplished a success rate of 66.7%; the remaining cases required surgery for vaginal bleeding and one case developed sepsis (11). Our patient presented 4 days after the fetal intracardiac KCL injection with sepsis and then developed severe vaginal bleeding requiring emergency D&C. Upon presentation, leukopenia and neutropenia were evident; it is unclear if this was just a component of the sepsis or a side effect of MTX medication. Likewise, the blood culture showed *Peptostreptococcus asaccharolyticus* which most likely entered the blood during the transvaginal needle insertion into the gestational sac. These bacteria are gram-positive anerobic cocci that normally colonize mucocutaneous surfaces and are frequently isolated in obstetrics and gynecological sepsis (12). Bartlet et al. (1977) described that when they cultured the vaginal discharge of healthy women, peptococci and peptostreptococci were present in 73% of cases (13). Mikamo et al reported 2 cases of ovarian abscesses secondary to *Peptostreptococcus* species after ultrasound-guided transvaginal aspiration of endometriomas (14). An elevated degree of suspicion for infection should be maintained after invasive procedures.

What is more, intra-gestational sac MTX and KCL were given in 3 of our cases. Cheung's assessment of ninety-six cases of scar ectopic treated with local MTX exposed a success rate of 73.9% that climbed to 88.5 following administering an extra dose of local or systemic MTX with 11.5% requiring surgical management (15). In a review by Timor et al, the lowest complication rate (needing further intervention) with CSP treatment was in those treated by

intra-gestational sac MTX +/- KCL, occurring in 9.6% of cases. In contrast, this was not the case in our series in which all the cases required a second intervention after the intra-gestational sac therapy.

In our first experience, case 2, transabdominal intra-gestational sac MTX was provided after systemic MTX failed. On the second day, persistent fetal cardiac activity was noticed; therefore, intra-gestational sac KCL was administered, and asystole was confirmed. Afterward, the patient did not need any further treatment. Considering the other 2 cases (cases 4 and 5), we opted to combine intra-gestational sac MTX and KCL together with a good response. One patient (case 5) needed one extra dose of systemic MTX for slowly declining β-hCG, and both required a D&C for persistent bothersome vaginal bleeding secondary to the RPOC. Numerous studies have previously used a combination of intra-gestational sac MTX and KCL in conjunction with positive results (16–18).

Due to the high likelihood of complications like bleeding and perforation, D&C is not advised to be used alone as a main therapy for CSP. Bleeding occurs due to injury of the highly vascular bed of the CSP.[1] Interval ultrasound guided D&C for persistent symptoms appears to be safe with minimal blood loss as demonstrated in our cases (cases 3-5); the mean interval between the medical treatment and D&C was 12 weeks (range 6-20 weeks). All patients had a low β-hCG level before the curettage (range 1.2-9.9 IU/L). Wang et al suggested that the best time to perform a D&C after MTX treatment is when the β-hCG level is below 50 IU/L with the absence of Doppler flow in the gestational sac (19).

Finally, we had one successful pregnancy after the cesarean scan ectopic. Wu et al conducted a systematic review on 3380 scar pregnancies, where 538 resulted in pregnancy. Among them, 33% had a successful delivery and 15.3% experienced recurrent scar pregnancy. The review did not establish if the various treatment methods had any impact on pregnancy outcomes (20).

Limitations of the Study

This retrospective study was conducted at a single center and had a small sample size, which is attributed to the low incidence of cesarean scar pregnancy. Since only medical treatment was administered and primary surgical methods were not used, there was no comparative group.

Conclusion

In conclusion, early ultrasound in patients with previous cesarean surgeries is advised to locate the pregnancy and manage accordingly. Systemic IM MTX as a first-line treatment for scar pregnancy should be avoided unless the pregnancy is failing or non-viable. Intra-gestational sac treatment can be associated with persistent retained products of conception leading to bothersome persistent vaginal spotting and an interval ultrasound guided D&C in type 1 CSP seems to be safe, though the exact interval needs to be established by further studies. Invasive medical treatment can be complicated with life-threatening sepsis and a high index of suspicion and prompt treatment is required.

Conflict of Interests

None.

Ethical Issues

This study was approved by the Unit of Biomedical Ethics at King Abdulaziz University Hospital (reference number 320-19), according to the relevant guidelines in Saudi Arabia and the ethical principles stated in the Declaration of Helsinki. The patient provided written consent for the publication and use of their ultrasound images for educational and research purposes. This was obtained through a voluntary signing of a research agreement form in the fetal medicine unit.

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