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Case Series

## Management and outcomes of caesarean scar pregnancy in medina maternity and children hospital

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### ABSTRACT

Undergoing previous cesarean section (CS) can have the possibility for implantation of embryonic sac of any later gestation throughout its scar evolving what was known as a scar pregnancy (SP). The aim of this study to describe the diagnosis, treatment and outcomes of caesarean SP in Medina maternity and children hospital. This a case series study encompassed all patient diagnosed and managed as caesarean SP in Medina maternity and children hospital, Medina (MMCH), Saudi Arabia in the period from January 2020 to January 2021. Demographics, clinical and discharge data were attained from the previous hospital electronic records, nursing notes, anesthesia sheets, operative notes, discharge papers, and outpatient clinic documents. A total of 11 women detected by ultrasound (US) and magnetic resonance imaging (MRI) as SP. The mean age of women was  $36\pm 3.8$  years. The median number of repeated CS was 2 while the mean gestational age was  $50.6\pm 7.8$  days. The interval from diagnosis to management ranged from 2 to 9 days with a median of 4 days, and the interval between start treatment and negative Beta human chorionic gonadotropin  $\beta$ -hCG ranged from 21 to 135 days with a median of 62 days. The mean interval from last CS until this pregnancy is  $39.7\pm 19.2$  months. Systemic methotrexate (MTX) given in a single dose for two patients while nine patients received multiple doses. Local MTX given for six cases. Bleeding as a complication occurred with two out of the eleven patients. MTX was actual treatment for SP, but bigger multicenter randomized-controlled trials involving more cases are essential to validate our conclusions.

**Keywords:** Cesarean, SP, Ultrasound, MTX

### INTRODUCTION

Cesarean section (CS) rate rose strikingly in the last decade reaching up to 21% of deliveries. The rise was reported on 29.7 million CS annually performed among 169 countries.<sup>1</sup> That growth advocated for a widespread of indicated "first" CS use from 12.6% to 20.6% and a decrease in vaginal births after CS from 28% to 9.2% with a repeated incident of CS nowadays of around 91%.<sup>2</sup> Maternal adverse outcomes were greater after CS than following ordinary normal vaginal delivery. CS was claimed to be related to above average rate of ectopic pregnancy, placenta previa or accrete and ruptured uterus. Additionally, described outcomes has been linked in a

direct proportionate way with the number of CS.<sup>3</sup> CS extended the danger of gestational sac abnormal implantation during the consequent pregnancies on top of the cesarean scar, giving rise to what defined as SP that its danger level raised with repetitive CS.<sup>4</sup> Since 2000, SP recurrence demonstrated a critical flood, reaching 6.1% of every single ectopic pregnancy in ladies with prior CS, which may be appended to both extended aggregate of CS as well as the improved detection rate of ectopic pregnancy.<sup>5</sup>

In SP, intrusion of the sac into the myometrium happens due to dehiscence or a scar imperfection because the lower uterine segment develop fibrosis and has poor

vascularization.<sup>6</sup> The area of CS scar in most of complicated women is defective, especially after numerous CSs. The scar surface usually expands, and the front uterine wall can have inadequate blood supply due to fibrosis and impeded recuperating. In fact, 72% of women with SP revealed by this creator had multiple CSs. In the previously performed surgeries, double layer sutures are applied which results in modifying the principal layer continuously. A single non-reversing running suture, as normally utilized sometimes, may prompt disabled postoperative convalescing as well as formation of deformities inside the scar.<sup>7</sup> The aim of this study is to represent the data of a tertiary care center with the recognizable proof as well as care of SP and to examine patients' difficulties identified with this uncommon sort of ectopic pregnancy. Previous report of SP occurrence was between 1:1,800 and 1:2,216 pregnancies, it comprises 6.1% of every single ectopic pregnancy with a past filled with at any rate one CS.<sup>8</sup>

Few strategies were utilized to analyze uterine SPs. Transvaginal ultrasound (TVS) assessment was the essential analytic way in a list of specific criteria.<sup>9</sup> Those include visualization of a void uterine hole just as a void endocervical waterway, placenta detection as well as an embryonic sac, earlier of  $\leq 8$  weeks a triangular sac that fills characteristically the scar, after 8 weeks the shape may be adjusted to oval, cylindrical (1-3 mm) or missing myometrium separating the sac from urinary bladder, closed hole cervix, undeveloped fetal pole $\pm$ yolk sac $\pm$ heart activity and powerful vascular network around CS scar zone.

Methotrexate (MTX) is a folinic acid agonist involved in the processing of DNA production. It is given in ectopic pregnancy and choriocarcinoma because it can halt the activity of highly proliferative cells. Unfavorable effects include stomatitis (5%), diarrhea (14%), vomiting (17%) and nausea (50%).<sup>19</sup> MTX can be used systemically for tubal pregnancies, principally or unruptured early phase with a 90% success rate. However, systemic MTX administration is less effective in pulsating tubal pregnancies as well as cervical or cornual ones.<sup>10</sup> Gestational sac aspiration with the administration of methotrexate into the sac combined with systemic administration of methotrexate appears to have a better success rate and requires fewer additional interventions. In a review of 17 reported cases, 74% of the women treated with this combined method required no further interventions.<sup>10</sup> On the other hand, uterine artery embolization (UAE) has been used in conjunction with the administration of systemic or local methotrexate and during or after surgical removal of SP to prevent bleeding and have similar good rates of success.<sup>11</sup>

Cervical dilatation and curettage are a commonly used method of managing SP. Surgical evacuation is suitable for endogenous SP with a myometrial thickness of at least 2 mm. However, it carries the risk of bleeding and may fail to remove all of the pregnancy sac residues in the scar

tissue. It should be performed under the guidance of ultrasound to aid complete tissue removal. Various techniques to reduce bleeding during and after surgical evacuation have been reported. Most case series have reported the use of UAE with methotrexate, but other reported techniques include the use of intrauterine Foley's catheter and Shirodkar's sutures. A Shirodkar's suture applied prior to suction evacuation and tied after the procedure is an effective method of reducing bleeding following evacuation. It also avoids the risks of further intervention such as UAE and preserves future fertility.

## CASE SERIES

This is a case series study that was done from January 2020 to January 2021 at maternity and children hospital (MMCH) in Madinah, Saudi Arabia. The study was approved by the institutional review board of the hospital and all patients provided a written informed consent to participate in this study. We surveyed the electronic records of all patients admitted to obstetrics and gynecology department who were diagnosed with SP. Recruited women assented before beginning information arrangement and complete advising about potential perils up to hysterectomy. All patients were educated regarding each modality and their side effects. SP addressed through meticulous woman's history including obstetric, conceptive, clinical and careful history just as physical assessment. The data collected were fortified by the accompanying ultrasound which reported vacant uterus, CS scar approached by sac or placenta, reedy (thickness  $< 4$  mm) or missing myometrium between sac and bladder, triangular-shaped sac within the scar (as early as  $\leq 8$  weeks) that move to get adjusted or once in a while oval at  $> 2$  months, embryonic fetal post $\pm$ yolk sac $\pm$ cardiovascular action, sealed and abandoned endocervical channel or high vascular example around CS scar. Afterwards, confirmation of the diagnosis and the US was done by conduction a magnetic resonance imaging (MRI).

Treatment options were offered to each patient after the diagnosis of SP. Details of the advantages and complications of each treatment was provided. Patients were monitored by pelvic examination,  $\beta$ -hCG test and ultrasonography in our outpatient clinic once in a week regularly until a negative  $\beta$ -hCG result is confirmed after the treatment.

The management included intramuscular (IM) MTX 100 mg with re-evaluation one week later by B-HCG and ultrasonography. If  $\beta$ -hCG did not decline or the fetal heart was still positive, we gave a second dose of IM MTX 100mg with another evaluation one week later. If  $\beta$ -hCG did not decline or fetal heart still positive, offered a local MTX 100 mg with weekly outpatient clinic follow up.

Data included age, parity, body mass index (BMI), gestational age, interval between last cesarean delivery CD and SP, clinical presentation, general situation, interval between diagnoses and treatment,  $\beta$ -hCG titer, ultrasound

and MRI finding, type of treatment and Outcome. Descriptive statistics were done using frequency and percentages for the categorical data, and using min max, median, mean, standard deviation for numeric variables.

A total of 11 participants were included in the study and the SP was distinguished by US and MRI. The mean age of the women was 36±3.8 years. And the mean BMI was 27.7±5.4. The mean gestational age of SP at time of diagnosis was 50.6±7.8 days. The minimum number of previous CS was one while the maximum was five with a median of two previous CS (Table 1).

The mean interval from last CS until this pregnancy was 39.7±19.2 months. The interval from diagnosis to the

management ranged from two to nine days with a median of four days. The mean value of β-hCG level at start of treatment was 76313.8±76089.3 mIU/mL, and the interval between treatment and negative β-hCG ranged from 21 to 135 days with a median of 62 days (Table 1). The general condition for all eleven patients was stable, three patients were asymptomatic while six complained of vaginal bleeding, and two cases complained of pain. There was a fetal pole in seven cases and positive fetal heart in seven cases (Table 2). Systemic MTX given in a single dose for two patients while nine patients received multiple doses. Local MTX given for six cases. Bleeding as a complication occurred with two out of the eleven patients that managed by suction curettage under US guidance (Table 3).

**Table 1: Women’s history and examination.**

Variables	Minimum	Median	Maximum	Mean	SD
Age (years)	30	37	43	36.0	3.8
Hight (cm)	149	155	165	155.9	4.6
Weight (kg)	50.0	68.2	89.0	67.4	13.3
BMI (kg/m <sup>2</sup> )	22.2	27.7	37.0	27.7	5.4
Parity	2	4	8	4.1	2.1
Abortion	0	1	4	1.3	1.3
No. of CS	1	2	5	2.5	1.3
GA (days)	42	48	70	50.6	7.8
Interval from diagnosis till management (days)	2	4	9	4.8	2.6
Interval from last CS till this pregnancy (months)	12	38.00	72	39.7	19.2
B-HCG at start of treatment	372	42992	261760	76313.8	76089.3
Interval between treatment and -ve B-HCG (days)	21	62	135	63.9	31.3

**Table 2: Women’s clinical characteristics.**

Variables	Frequency	Percent (%)
Parity	2	36.4
	3	9.1
	4	9.1
	5	27.3
	7	9.1
	8	9.1
Abortion	0	27.3
	1	45.5
	2	9.1
	3	9.1
	4	9.1
No. CS	1	18.2
	2	45.5
	3	9.1
	4	18.2
	5	9.1
Complaint	Asymptomatic	27.3
	Vaginal bleeding	54.5
	Pain	18.2
General condition	Stable	100

Continued.

Variables		Frequency	Percent (%)
<b>Interval from diagnosis to management (days)</b>	2	1	9.1
	3	3	27.3
	4	4	36.4
	8	1	9.1
	9	2	18.2
<b>Fetal pole</b>	No	4	36.4
	Yes	7	63.6
<b>FH</b>	Negative	4	36.4
	Positive	7	63.6
<b>MRI</b>	Confirmed	11	100

**Table 3: Study management outcomes.**

Variables		Frequency	Percent (%)
<b>Systemic MTX</b>	Single dose	2	18.2
	Multiple doses	9	81.8
<b>Local MTX</b>	No	5	45.5
	Yes	6	54.5
<b>Complication</b>	No complication	9	81.8
	Bleeding	2	18.2

## DISCUSSION

SP is an uncommon ectopic pregnancy and its frequency in our center could be risen due to the upsurge of the CS rate. During study period, the rate of CS was 33.2% and the frequency of SP was 0.22% (11/5042 CS). There are two justifications of this increase, initially, as a tertiary care center, several women suffering complicated pregnancies as ectopic or SP were referred for supervision. Moreover, new advances of TVS with higher frequency probes that permitted earlier identification of such conditions. Improved detection as well as peak of the number of CS are apparently accountable for that upsurge of SP. The biological history of SP disorder is undetermined, but unprompted early scar rupture in pregnancy and bleeding, if the pregnancy could continue, with the probable hazardous maternal undesirable outcomes.

Endometrial as well as myometrial disfiguring or disturbance might lead the growing embryo into an implantation defect. In addition, inadequate decidualization could result in trophoblast invasion or adherence to the lower uterine segment. Nevertheless, the difference between a pregnancy complicated with placenta accreta to that of SP is that in the later sac it would be embedded within the myometrium being completely separated from the hollow cavity. Developing a microscopic pathway inside the fibrous CS scar was the method that mostly could describe myometrial implantation and invasion. Such pathway was mostly a direct result of a prior surgical trauma of any cavitary surgery as CS, curettage, myomectomy, removal of the placenta manually or even office hysteroscopy.<sup>8</sup> The time

interval amid trauma with subsequent pregnancy could influence implantation as many documented conditions recorded only few months following a CS hinting that partly healed the surgical wound aided the scar implantation.<sup>12</sup>

Veridiano et al illustrated a difficult case following delivery which was complicated by placenta per Creta that suffered spontaneous uterine perforation at 14 weeks' gestation in the subsequent pregnancy and was managed by emergency hysterectomy following severe hemorrhage.<sup>13</sup> Furthermore, Herman et al was the first to utilize US to describe case of 1<sup>st</sup> trimester sac implanted within a CS scar.<sup>6</sup> Her pregnancy was uneventful, but the patient was delivered by emergency CS and a hysterectomy was performed due to serious blood loss that led to coagulopathy.

Firm US standards used to distinguish SP as empty cavity, empty cervical canal, anterior isthmic gestational sac and an absent healthy myometrial layer between it and the urinary bladder.<sup>14</sup> Some physicians advocated an extra principle of high peri-trophoblastic blood flow around SP.<sup>15</sup> Lai et al described complexity, early on the 7<sup>th</sup> week of gestation, in finding the difference between a tubal ectopic pregnancy or in the myometrium of a prior CS. They recommended laparoscopic approach for the problem.<sup>16</sup> On the other hand, Godin et al advised with MRI use to confirm SP.<sup>7</sup> Its use or imaging by three-dimensional color Doppler could improve the accuracy of detecting SP by measuring the flow velocity, vascular indices among the peri-trophoblastic vascular bed; yet, representations might still be like those of placenta accrete shown late in pregnancy.<sup>4</sup> Due to the rarity of the disorder, most SPs published in form of case reports or few case series without agreement on the favorite management plan. Mostly, first trimester pregnancy termination clearly practiced preventing lethal problems.<sup>12</sup> Management goals must be directed to implement feticide prior disturbance, losing the gestation sac and maintaining the woman's potential fertility.

MTX was primarily utilized in treating ectopic pregnancy with the following prerequisites: when gestational age (<9 weeks), less than 10 mm fetal pole size and no evidence of cardiac activity was detected with <10,000 IU/L serum  $\beta$ -hCG levels.<sup>17</sup> Using MTX for SP management remained controversial, some used it in single systemic manner,

while others claimed it should be in multiple doses to achieve complete resolution.<sup>9,18-20</sup> It was primarily an accessory to hysterotomy as well as other procedures. Hypothetically, poor vascularity and fibrous tissue surrounding SP significantly limited the concentration of MTX within the lesion. Our results showed that most of the participants responded satisfactorily to systemic MTX. Rotas et al asserted sixteen women who were managed by IM MTX, 36% with ( $\beta$ -hCG <5,000 mIU/mL) resolved straightforward within few months and 36% got multiple MTX doses with oscillating leucovorin administration while two cases were complicated with bleeding which was controlled by surgical intervention.<sup>21</sup>

In our study, the median resolution time for SP in our results was 62 days that ranged from 21 to 135 days. Wu et al noted the  $\beta$ -hCG level decrease in women getting IM MTX was slow, and 16% had a  $\beta$ -hCG level drop by 50% following the first MTX injection.<sup>22</sup> Yang et al also discovered that the decline time was long in SP women getting IM MTX only.<sup>23</sup> Two of our participants (18.2%) needed just single MTX course, while double doses were required in other nine (81.8%) with six (66.6%) of them requiring local MTX. Regarding the use of  $\beta$ -hCG level as marker for requiring supplementary therapy, Chen et al reported a  $\beta$ -hCG decline of 68.3% and 49.6%.<sup>24</sup> After one week of MTX, 33,082 mIU/mL was  $\beta$ -hCG level after treatment in the latter case that necessitated other two extra systemic MTX courses. These data recommended that the dose and number of MTX injections mandatory should consider gestational age as well as the existence of an embryonic cardiac activity. Lastly, regardless the medical management of SP of 11 participants was effective, the assessment of MTX consequences depending on this number was insufficient for inducement of a final assumption concerning the usefulness of such protocol, especially without comparing with other existing choices. Therefore, considering CS rate rise, health workers should pay attention to the likelihood of this type of ectopic pregnancy in the woman's future pregnancies.

Limitation of our study include a small sample size despite having reviewed a large era of years. This small data does not represent the actual population. Furthermore, the nature of the paper is of descriptive due to the small number of patients included making a research on higher number on a multi-center level necessary to determine the correct factors associated with SP.

## CONCLUSION

MTX was the actual treatment for SP and was effective and efficient. Other treatment modalities did not show the same when compared to MTX. However, bigger multicenter randomized-controlled trials involving more cases are essential to validate our conclusion.

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