

Cesarean Scar Pregnancy and Morbidly Adherent Placenta: Different or Similar?

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ABSTRACT: **Background:** Growing evidence suggests that cesarean scar pregnancy (CSP) and morbidly adherent placenta (MAP) may represent a continuum of the same disease.

Objectives: To investigate and compare the prior risk factors in women with either CSP or MAP.

Methods: The study included 33 women diagnosed with CSP in our department between 2006 and 2014. For each CSP case, two pregnant patients with MAP were matched for hospitalization date from delivery ward records, constituting the control group.

Results: In both groups, maternal age, parity, and previous early and late abortions were similar. The rate of conception by assisted reproductive technologies was 9% in both groups. Although the number of previous cesarean sections was statistically different between CSP and MAP (2.0 ± 1.0 vs. 1.0 ± 1.0 , respectively, $P = 0.006$), the leading indication of previous cesarean section was breech presentation in both groups (28.1% and 27.8%, respectively, $P > 0.05$).

Conclusions: CSP and MAP share similar prior risk factors. Due to high morbidity in both diseases, further research is needed toward reducing the known etiological factors contributing to the growing number of both complications.

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The increased prevalence of cesarean section (CS) in the Western world has been associated with an increase in morbidly adherent placenta (MAP) in subsequent pregnancies [1,2]. Pathological implantation in a previous cesarean scar resulting in a cesarean scar pregnancy (CSP) is another iatrogenic complication of a previous cesarean delivery [3-8].

The rate of MAP (placenta accreta, increta and percreta) has gradually increased from 1 in 30,000 deliveries in the 1930s to 1 in 2000–3000 deliveries in the last decade [1,5]. Likewise, the rate of CSP is currently estimated at 1 in 800–2500 women with a previous cesarean delivery [5].

Multiple cesarean deliveries have been suggested as a strong risk factor for CSP [9-12,13]. Our finding that 50% of women

presenting with CSP had undergone at least two cesarean deliveries was similar to previous reports [3,12]. Placenta previa and previous uterine surgery represent the major risk factors for MAP [1]. The women at risk for CSP appear to be those with a history of placental pathology, ectopic pregnancy, multiple cesarean sections, and cesarean breech delivery [3,4,13]. Growing evidence suggests that CSP and MAP are not separate entities but may represent a continuum of the same condition [8,9].

We aimed to investigate and compare the prior risk factors in women with either CSP or MAP and to provide further proof for the hypothesis that these two conditions could share similar prior risk factors that may contribute to a single iatrogenic complication. To the best of our knowledge no other work has addressed this issue.

PATIENTS AND METHODS

We performed a computerized database search for cases with CSP that had been diagnosed in our department during the years 2006–2014. The study cohort consisted of 33 women with a diagnosis of CSP during the study period. All fulfilled the sonographic criteria for CSP diagnosis and some took part in our previous study on this subject [3,4,10,11,13]. The sonographic criteria for a CSP diagnosis are: (i) an empty uterus, (ii) an empty cervical canal, (iii) the gestational sac being located in the anterior part of the isthmic portion of the uterus with a diminished myometrial layer between the bladder and the sac, and (iv) a discontinuity in the anterior wall of the uterus demonstrated on a sagittal view of the uterus when the direction of the ultrasound beam runs through the amniotic sac [3,4,10,11,13].

The medical records of all identified cases were retrospectively reviewed, and data regarding demographics, obstetric and gynecologic history were collected. For each of these cases, two consecutive cases with surgically confirmed MAP were retrieved from the department's computerized database (control group). We chose one MAP patient who was diagnosed and treated prior to each CSP case and one MAP case immediately following the same CSP case.

Statistical analysis was performed in the statistical laboratory at Tel Aviv University using SPSS software (SPSS Inc., version 15, Chicago, IL, USA). Continuous variables are presented as the mean \pm standard deviation or as median (range).

Frequencies are presented as percentages. For comparison of continuous variables, the Mann-Whitney rank test and the Student *t*-test were used. The chi-square test was used to assess frequencies. Double-tailed *P* value < 0.05 was considered statistically significant. The study was approved by the Institutional Review Board.

RESULTS

A total of 99 women were enrolled in the current study: 33 women with a CSP and 66 women with MAP. The characteristics of CSP and MAP patients are presented in Table 1. There were no differences in age, parity, mode of conception, or previous early and late abortions between the two groups. However, there was a significant difference in gravidity in women with CSP compared to women with MAP (6 ± 3.8 vs. 5 ± 2.6 respectively, $P = 0.029$) [Table 1].

Although the number of previous cesarean sections were statistically different in women with CSP versus MAP (2.0 ± 1.0 vs. 1.0 ± 1.0 respectively, $P = 0.006$), the leading indication for previous cesarean section was breech presentation in 28.1%

and 27.8% respectively ($P > 0.05$). Furthermore, the duration of hospitalization in the current pregnancy was significantly longer in women with MAP compared to CSP (6.1 ± 3.5 vs. 2.2 ± 1.1 days, $P < 0.001$) [Table 1]. There was no difference in type of previous CS uterine incision between the groups. Finally, the time interval from the previous CS to the current complication was similar in both groups.

DISCUSSION

The main finding of the present study was that the demographic, obstetric and gynecologic history of women with CSP and those with MAP was similar. There were similar assisted reproductive technology rates for conception in both groups. Finally, our study further reinforces the theory that there is a common underlying causal relationship between CSP and MAP [2].

We previously described the methods for treatment of SCP [3,4]. The treatment methods are as follows: conservative follow-up, transcervical aspiration of the gestation sac under ultrasound guidance, intra-amniotic methotrexate (MTX) injection, and surgical removal of the ectopic pregnancy, with or without hysterectomy after removal of the pregnancy.

The high rate of CS due to breech presentation and the subsequent occurrence of CSP and MAP is another intriguing association that we encountered in our study. This association might not be coincidental [5]. Another remarkable finding in our study was a similar time interval from a previous CS to the current complication (CSP or MAP). Our findings showed that many of these operations are currently elective procedures performed in a non-developed lower uterine segment, so that the healing process following the surgery might facilitate implantation of the blastocyst within the scar. We propose that the increasing number of cesarean sections for various indications [12] together with changes of the surgical technique [3,4] and its indications [3,4] might contribute to the increase in cesarean scar implantation. These possibilities need to be further explored.

Interestingly, we found a similar rate of women with previous corporeal uterine incision between the two entities. Whether any specific surgical technique such as single- or double-layer closure of the incision can prevent CSP or MAP is still an open question. There are numerous articles devoted to the different incision closure techniques. Most are summarized in a Cochrane Database report reviewing 30 studies [12]. None of them, however, was designed to address whether the type of surgical technique can influence the occurrence of CSP or MAP.

Rosen [13] reviewed the subject of the CSP and placenta accreta, discussing some of the theories behind their pathophysiology. In vitro work demonstrated the role of a low oxygen tension, which seems to be an important prerequisite for the

Table 1. Characteristics of the cesarean scar pregnancy and morbidly adherent placenta groups

	Cesarean scar pregnancy (n=33)	Morbidly adherent placenta (n=66)	P value
Age (yr), mean ± SD	36.3 ± 4.7	34.8 ± 3.8	NS
Mode of conception (%)			
Spontaneous	90.9%	90.1%	NS
Assisted reproductive technologies	9.1%	9.4%	
Obstetric history			
Gravidity (mean ± SD)	6 ± 3.8	5 ± 2.6	0.029
Parity (mean ± SD)	3 ± 1.3	2 ± 1.7	NS
Previous CS (mean ± SD)	2 ± 1.0	1 ± 1.0	0.006
Previous CS indication (%)			
Elective CS	50.0	59.3	NS
Emergent CS	21.9	13.0	
Breech presentation	28.1	27.7	
Previous low segment transverse uterine incision (%)	93.1	96.2	NS
Previous corporeal uterine incision (%)	6.9	3.8	NS
Previous FMA (%)	6.1	1.5	NS
Previous SMA (%)	3.0	0	NS
Previous FIA (%)	3.0	1.5	NS
Previous SIA (%)	3.0	0	NS
Duration of hospitalization in the current pregnancy (days), mean ± SD	2.2 ± 1.1	6.1 ± 3.5	< 0.01
Time interval from previous CS to primary event diagnosis (yr), mean ± SD	3.6 ± 3.3	3.8 ± 2.02	NS

FMA = first-trimester missed abortion, FIA = first-trimester induced abortion, SMA = second-trimester missed abortion, SIA = second-trimester induced abortion, CS = cesarean section

invading cytotrophoblast to proliferate, thereby regulating placental growth and its architecture [14,15]. The scar tissue into which the placenta implants may provide that exact environment of low oxygen tension necessary to stimulate the cytotrophoblast to deeply invade the scarred area [16]. Opposing views may offer a different explanation regarding implantation into the scar. In vitro studies with trophoblast and endometrial explants have shown that a trophoblast has a stronger propensity for attaching to exposed extracellular matrix than endometrial epithelial cells [17]. This incidence may explain why blastocysts have a preference to exposed scar tissue, which is denuded of epithelial cells. This theory may explain the observation that the higher the rate of previous cesarean sections, the higher the risk of MAP and CSP, both because of areas of denuded scar tissue exposed to the blastocyst.

In light of the trend toward increased cesarean deliveries, the likelihood of such remote complications is expected to increase. Therefore, the issue of reducing CSP/MAP cases must be addressed. Currently, with the advent of transvaginal sonography and use of saline infusion, the integrity of the uterine wall can be detected even in the non-pregnant state [18]. A cesarean scar defect, defined by the presence of fluid within the incision site [17], or any filling defect (“niche”), defined as a triangular anechoic structure at the presumed site of a previous cesarean scar [18], might indicate uterine scar complications in a subsequent pregnancy [6]. According to Jauniaux and Jurkovic [6], a scar is deficient when there is a visible gap in the anterior uterine wall covered by a thin layer of peritoneum, or when there is loss of more than 50% of the myometrial thickness compared to the myometrium adjacent to the scar. However, severely deficient uterine scars are not that rare. One study detected them in 10% of a population of women with histories of previous cesarean deliveries [19]. A policy of routine defective cesarean scar repair would result in a large number of operations, which would be costly and difficult to justify. Such a protocol could also lead to various complications, such as poor scar healing, adhesion formation, and even hysterectomy, which could be detrimental to women’s future fertility. Furthermore, repair of the uterine scar may not prevent the occurrence of uterine rupture in a subsequent delivery [20]. In light of the above considerations, we believe that surgical repair should be reserved only for highly select cases, perhaps for women with unusually large uterine defects [21]. There are also indications that some authors have recognized the need for early diagnosis of MAP [18,22-24]. This would enable early counseling and intervention, preventing complications or loss of the uterus. Management of high risk patients is a particular concern. Seow and collaborators [25] reported detecting a scar defect by transvaginal sonography 4 years prior to a patient’s in vitro fertilization (IVF)-induced pregnancy. This scan might be important for the subgroup of women at risk for CSP, as

reported previously. Those authors [25] also recommended that for IVF pregnancies in patients with a history of a cesarean delivery, embryos should be transferred more than 4 cm from the cervix to avoid either cesarean scar pregnancy or cervical pregnancy. Our management of subsequent pregnancies mirrored the process described in the literature [4,5] and included early sonography to confirm the intrauterine pregnancy location as well as sonography to monitor fetal growth and exclude abnormal placentation.

In conclusion, CSP and MAP share similar prior risk factors and provide further proof for the hypothesis that these two conditions may represent a continuum of the same disease. Findings regarding the risk factors might contribute to prevention and early diagnosis of the disease. Therefore, the recommendation that clinicians raise the possibility of CSP/MAP with the sonographer by providing a history of cesarean delivery on the referral letter is particularly important. Further studies and more investment should be directed toward reducing the known etiological factors that may contribute to the rapidly growing number of both CSP and MAP.

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