



Cesarean scar pregnancy is a precursor of morbidly adherent placenta

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ABSTRACT

Objective To provide further sonographic, clinical and histological evidence that Cesarean scar pregnancy (CSP) is a precursor to and an early form of second- and third-trimester morbidly adherent placenta (MAP).

Methods This is a report of 10 cases of CSP identified early, in which the patients decided to continue the pregnancy, following counseling that emphasized the possibility of both significant pregnancy complications and a need for hysterectomy. Pregnancies were followed at 2–4-week intervals with ultrasound scans and customary monitoring. The aim was for patients to reach near term or term and then undergo elective Cesarean delivery and, if necessary, hysterectomy. Charts, ultrasound images, operative reports and histopathological examinations of the placentae were reviewed.

Results The ultrasound diagnosis of CSP was made before 10 weeks. By the second trimester, all patients exhibited sonographic signs of MAP. Nine of the 10 patients delivered liveborn neonates between 32 and 37 weeks. In the tenth pregnancy, progressive shortening of the cervix and intractable vaginal bleeding prompted termination, with hysterectomy, at 20 weeks. Two other patients in the cohort had antepartum complications (bleeding at 33 weeks in one case and contractions at 32 weeks in the other). All patients underwent hysterectomy at the time of Cesarean delivery, with total blood loss ranging from 300 to 6000 mL. Placenta percreta was the histopathological diagnosis in all 10 cases.

Conclusion The cases in this series validate the hypothesis that CSP is a precursor of MAP, both sharing the same histopathology. Our findings provide evidence that

can be used to counsel patients with CSP, to enable them to make an informed choice between first-trimester termination and continuation of the pregnancy, with its risk of premature delivery and loss of uterus and fertility. Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

INTRODUCTION

The rates of Cesarean delivery (CD), Cesarean scar pregnancy (CSP) and the different degrees (accreta, increta and percreta) of morbidly adherent placenta (MAP), also known as placental attachment disorders, have increased in a parallel fashion in the last decade^{1–11}. However, while there was a leveling-off in the number of CDs in the USA in 2012³, similar trends for CSP and MAP have yet to materialize.

The current literature documents that if management of CSP is expectant, some gestations will encounter severe maternal morbidity, such as massive intra- or postpartum hemorrhage, shock, intra-abdominal bleeding, a need for massive transfusion and uterine rupture with fetal loss, leading in most, if not all, cases to hysterectomy¹⁰. In addition, some gestations diagnosed as CSP in the first trimester have been reported to continue to late preterm or early term and to result in live offspring; however, in all published cases, the end result has been hysterectomy due to MAP, with permanent loss of fertility^{12–17}.

In 2012, Sinha and Mishra¹⁶ reported two cases of CSP with contrasting outcomes. The first had a complicated first-trimester course, requiring two dilatation and curettage procedures for evacuation of products of conception, laparoscopy and intramuscular methotrexate administration; the second patient continued the pregnancy and at

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37 weeks underwent elective CD for placenta previa with suspected accreta. The delivery was complicated by MAP and massive postpartum hemorrhage, and hysterectomy was performed. The histology of the placenta was consistent with placenta increta. Based upon their reading of the literature and the histology of these two cases, Sinha and Mishra hypothesized that CSP and MAP are not separate entities but 'rather a continuum of the same condition'. In another recent article, Ballas *et al.*¹⁵ reported that in 10 cases with gestational ages between 8 and 14 weeks, the gestational sacs were located in the lower uterine segment and fulfilled the diagnostic criteria of CSP. These women went on to deliver live offspring, but each lost her uterus due to MAP.

Three additional published case reports^{12,14,17} describe cases with a sonographic diagnosis of CSP in which the pregnancy continued to near term, with similar outcomes to the cases described by Sinha and Mishra¹⁶ and Ballas *et al.*¹⁵. Comstock *et al.*¹⁸ found, on retrospective examination of first-trimester scans of patients who had second- and third-trimester MAP, that there were ultrasound findings consistent with early accreta, which they termed 'scar pregnancy'. In our recent study¹⁹, pathologists evaluated cases of CSP and early placenta accreta in the late first and early second trimesters and confirmed that CSP and MAP have histopathological features that are indistinguishable from each other. We propose that there is a continuum, or spectrum, of placental attachment disorders, starting with CSP, progressing to early placenta accreta and eventually resulting in MAP, classically seen in the late second and third trimesters. While cases may have different clinical presentations, they all share the same histology¹⁹.

It thus appears that if CSP is managed expectantly in the first trimester and the pregnancy continues into the

second trimester, it is likely to evolve into MAP, leading almost unavoidably to a peripartum hysterectomy. It should be made clear, however, that not all patients diagnosed with MAP will necessarily lose their uterus. Leaving the placenta in place after cutting the cord at its placental insertion has been suggested as a management option in patients desirous of retaining fertility²⁰. Chandraran *et al.*²¹ have also described their uterus-sparing 'Triple P procedure'.

In this study, we present 10 patients in whom first-trimester diagnosis of CSP was well documented and established and who, after extensive counseling, elected to continue the pregnancy. We detail the diagnostic process and present their sonographic findings, clinical course, delivery and obstetric outcome. Our goal was to provide further proof for the hypothesis that CSP is a precursor of MAP and that CSP is the initial event in the continuum of MAP from the first to the second and throughout the third trimester of pregnancy.

SUBJECTS AND METHODS

We identified 10 patients with CSP, presenting during a 2-year period to our centers, who expressed their desire to continue their pregnancy. The ultrasound diagnosis of a CSP was established using sonographic features that we have described previously^{14,22}: (1) an empty uterine cavity and an empty endocervical canal; (2) the placenta and/or a gestational sac embedded in/on a hysterotomy scar; (3) in early gestations (< 8 weeks), a triangular gestational sac filling the niche of the scar; at > 8 weeks (all gestational ages in this paper are postmenstrual weeks) this shape may become rounded or even oval; (4) a thin (1–3-mm) or absent myometrial layer between gestational sac and

Table 1 Demographic and clinical data, outcome and histopathological results of 10 patients with Cesarean scar pregnancy who chose to continue the pregnancy and attempt to deliver live offspring

Case	Previous CD (n)	Age (years)	Last-index pregnancy interval (m)	GA at Dx (wks)	Antepartum complications	GA at delivery (wks)	Weight at delivery (g)	HAB	Total bleeding (mL)	Histology	Outcome/ observations
1	1	41	59	6 + 3	None	35	2580	+	800	Percreta	LB
2	1	27	38	9 + 2	None	36	2450	+	1100	Percreta	LB
3	1	37	21	5 + 4	None	36	2850	+	900	Percreta	LB
4	1	37	26	6 + 4	None	34	2600	+	1300	Percreta	LB
5	2	44	52	6 + 4	Bleeding at 33 wks	34 + 1	2650	+	1300	Percreta	LB
6	1	32	25	6 + 1	Severe bleeding at 19 wks, short Cx, TAH at 20 wks†	20	266	+	300	Percreta	TOP
7	2	35	141	6 + 5	Unknown‡	37	2120	+	6000	Percreta	LB, recvd blood and blood products
8	1	37	14	7 + 2	None	37	3300	-	300	Percreta	LB
9	1	40	48	6 + 5*	Contractions at 32 wks	32	1920	+	3000	Percreta	LB, recvd blood and blood products
10	1	27	12	7 + 2	None	34 + 1	2120	-	600	Percreta	LB, bladder injury

Hysterectomy was performed in all cases. *Diagnosis made at retrospective evaluation of images, after diagnosis of placenta accreta was made prospectively at 23 weeks. †Total abdominal hysterectomy (TAH) performed at 20 weeks' gestation, after uterine artery embolization and intracardiac administration of potassium chloride. ‡Lost to follow-up until 18 wks. CD, Cesarean delivery; Cx, cervix; Dx, diagnosis; GA, gestational age; HAB, hypogastric artery balloon (preventative placement); LB, live birth; m, months; Recvd, received; TOP, termination of pregnancy; wks, weeks.

bladder; (5) a closed and empty cervical canal; (6) an embryonic/fetal pole and/or yolk sac with or without heart activity; (7) a prominent and at times rich vascular pattern at or in the area of a Cesarean scar in the presence of a positive pregnancy test.

All patients were counseled extensively about the diagnosis and were offered termination of the pregnancy by one or more of the following methods: local intrages-tational and/or systemic injection of methotrexate; uterine artery embolization (UAE); aspiration of the gestational sac. These patients instead chose to undergo close ultrasound-based monitoring of the pregnancy in the hope of achieving a viable late preterm or early term delivery by elective repeat CD, with the understanding that a hysterectomy might be required. All patients agreed to this management plan. They were followed with serial ultrasound scans at 2–4-week intervals and, in some cases, with magnetic resonance imaging, as well as the customary pregnancy monitoring. Charts, serial ultrasound images, operative reports and histopathological examinations of these 10 patients were collected prospectively and were reviewed retrospectively for this study.

This research was approved by the institutional review board as an exempt study (study number S12-3237; 31 August 2012), because it involved the collection of existing data, document records and pathological/diagnostic specimens that are publicly available. Also, the information was recorded by the investigators in such a manner that subjects could not be identified, either directly or indirectly.

RESULTS

Table 1 details demographic and clinical data, outcome and histopathological results of the 10 patients. The

ultrasound diagnosis of CSP was made as early as 5 + 4 weeks and prior to 10 weeks in all but one case. The age at first ultrasound examination ranged from 5 + 4 weeks to 9 + 2 weeks. In one patient (Case 9) the diagnosis of CSP was made retrospectively by evaluating the scans performed at 6, 8, 11 and 15 weeks, after the diagnosis of MAP had been made prospectively at 23 weeks; the diagnosis could, in fact, be made retrospectively at the 6-week scan.

By the second trimester all patients exhibited most or all of the well-documented sonographic signs of MAP, namely: placenta previa, loss of the normal hypoechoic zone, interruption or alteration of the bladder line, placental lacunae, thinning of the myometrium at the uterine/bladder interface and increased vascularity on two- and three-dimensional color and power Doppler of the placenta^{23,24}.

The average age of the patients was 35.7 (range, 27–44) years. Eighty percent (8/10) of patients had only one prior CD and 20% (2/10) had two prior CDs. The average time between the last CD and the current pregnancy was 44 (range, 12–141 months).

Cases 1–5 were managed by the same maternal–fetal medicine specialist. The rest of the women (Cases 6–10) were treated by different specialists in different institutions. Nine of the 10 cases resulted in a liveborn neonate. The gestational age at delivery among the liveborn infants ranged from 32 to 37 weeks. Only three patients had antepartum complications. Patient 5 underwent bleeding at 33 gestational weeks and was delivered at 34 weeks; Patient 9 had contractions at 32 gestational weeks and was delivered then. In Case 6, ultrasound examination at 19 weeks detected a significant collection of blood and blood clots in the uterine cavity, with progressive

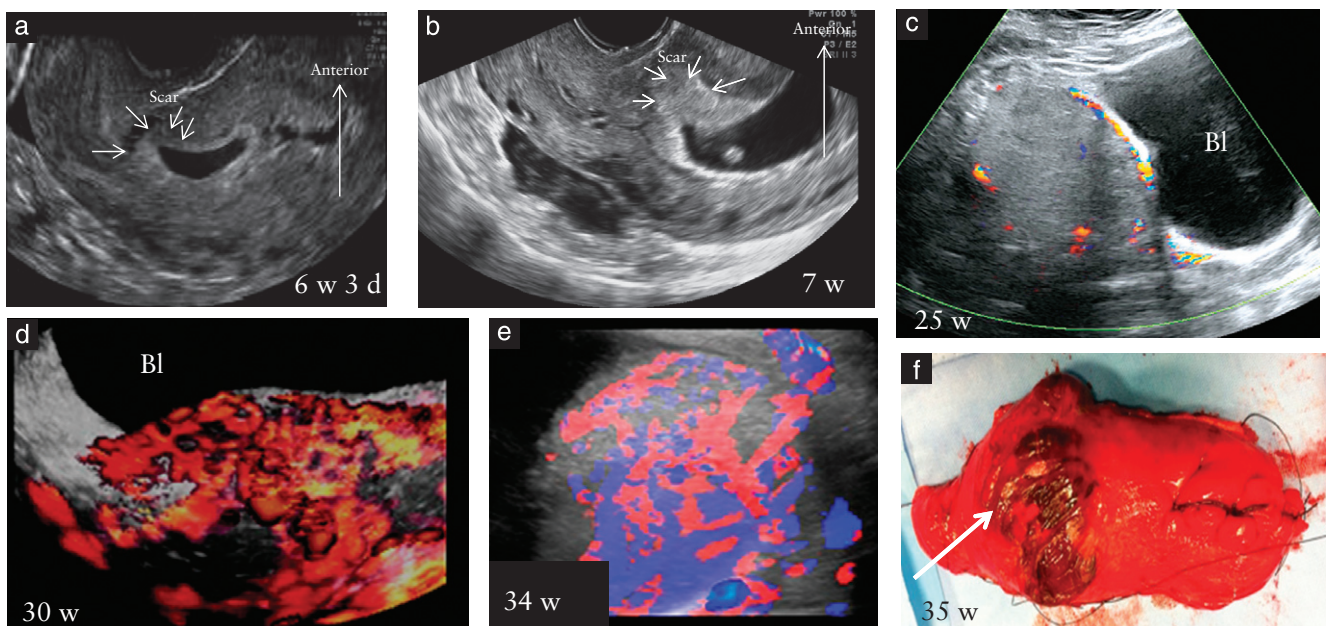


Figure 1 Case 1. (a,b) Gray-scale ultrasound images of Cesarean scar pregnancy at 6 + 3 weeks (a) and 7 weeks (b), with placental implantation on the scar indicated (small arrows). (c,d,e) Color Doppler imaging at 25 weeks (c), 30 weeks (d) and 34 weeks (e) was consistent with a morbidly adherent placenta. (f) The uterus, excised at 35 weeks, with the area of placental insertion indicated (arrow); histology was consistent with percreta. Bl, bladder.

shortening of the cervix. As a result, and with the blood loss being intractable, a total abdominal hysterectomy was performed at 20 weeks' gestation, after UAE and intra-cardiac administration of potassium chloride (KCl) to stop heart activity. At laparotomy, the paper-thin anterior uterine wall spontaneously ruptured and the cord was partially extruded.

All patients underwent hysterectomy, with preoperative prophylactic placement of bilateral balloon catheters into the hypogastric arteries using interventional radiology in all except two patients (Cases 8 and 10). Despite this balloon placement, the prior knowledge of the expected diagnosis and the planned surgical management, the mean blood loss was 1560 (range, 300–6000) mL. In almost all cases, the bleeding was due to neovascularization and significant pelvic adhesions, the surgical separation of the uterus from the bladder and parametrial involvement. Two patients (Cases 7 and 9) received large amounts of blood and blood products. Only one bladder injury was reported (Case 10). Placenta percreta was the histological finding in all 10 cases. Representative ultrasound images from each patient, as well as images of the excised uteri, are presented in Figures 1–5 and S1–S5.

DISCUSSION

In this study we report on nine patients with CSP identified early in pregnancy, and a tenth in whom this was done retrospectively following identification of MAP at 23 weeks, all of whom chose to continue the pregnancy and, if necessary, sacrifice their uterus in an attempt to deliver a live neonate. While patients were managed by different practitioners at different institutions using slightly different management protocols, in all cases there was a conservative but proactive approach, with close clinical and sonographic surveillance.

This paper provides important information useful for patient counseling. All patients were followed with serial ultrasound examinations and all demonstrated progression from the first-trimester CSP to sonographic findings typical of second-/third-trimester MAP. All except one patient delivered viable offspring late preterm or early term. Nine patients had Cesarean hysterectomy, most with significant blood loss, and in all cases the histological report confirmed the diagnosis of placenta percreta. One patient (Case 6) had intractable blood loss and cervical shortening leading to pregnancy loss and hysterectomy at

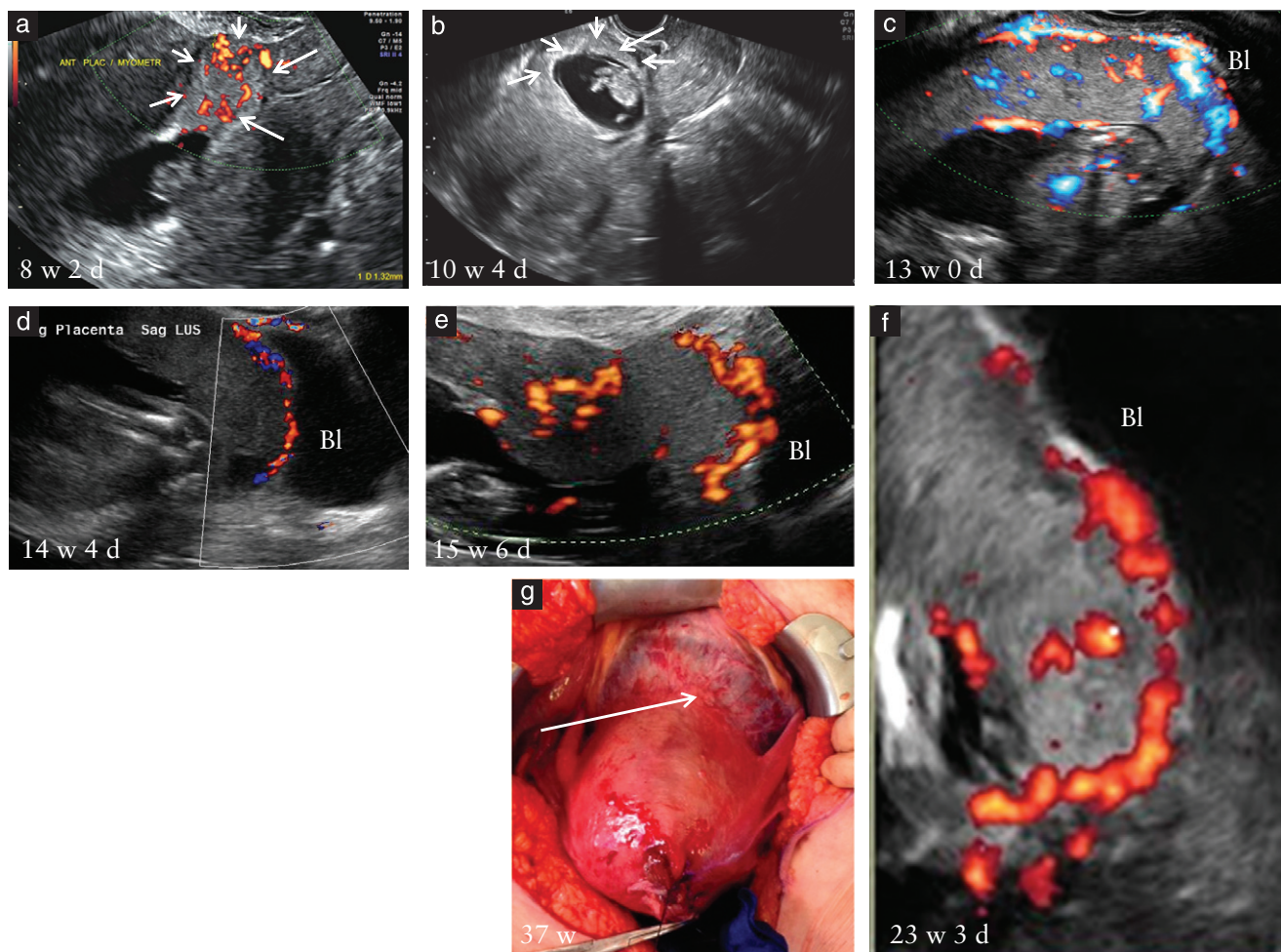


Figure 2 Case 8. Serial transvaginal gray-scale and color Doppler images of Cesarean scar pregnancy at 8 + 2 weeks (a) and 10 + 4 weeks (b), with placental implantation in the niche of the scar indicated (small arrows), as well as at 13 weeks (c), 14 + 4 weeks (d) and 15 + 6 weeks (e), and image of the morbidly adherent placenta at 23 + 3 weeks (f). (g) The uterus, excised at 37 weeks after Cesarean delivery, with placental invasion indicated (arrow); histology was consistent with percreta. Bl, bladder.

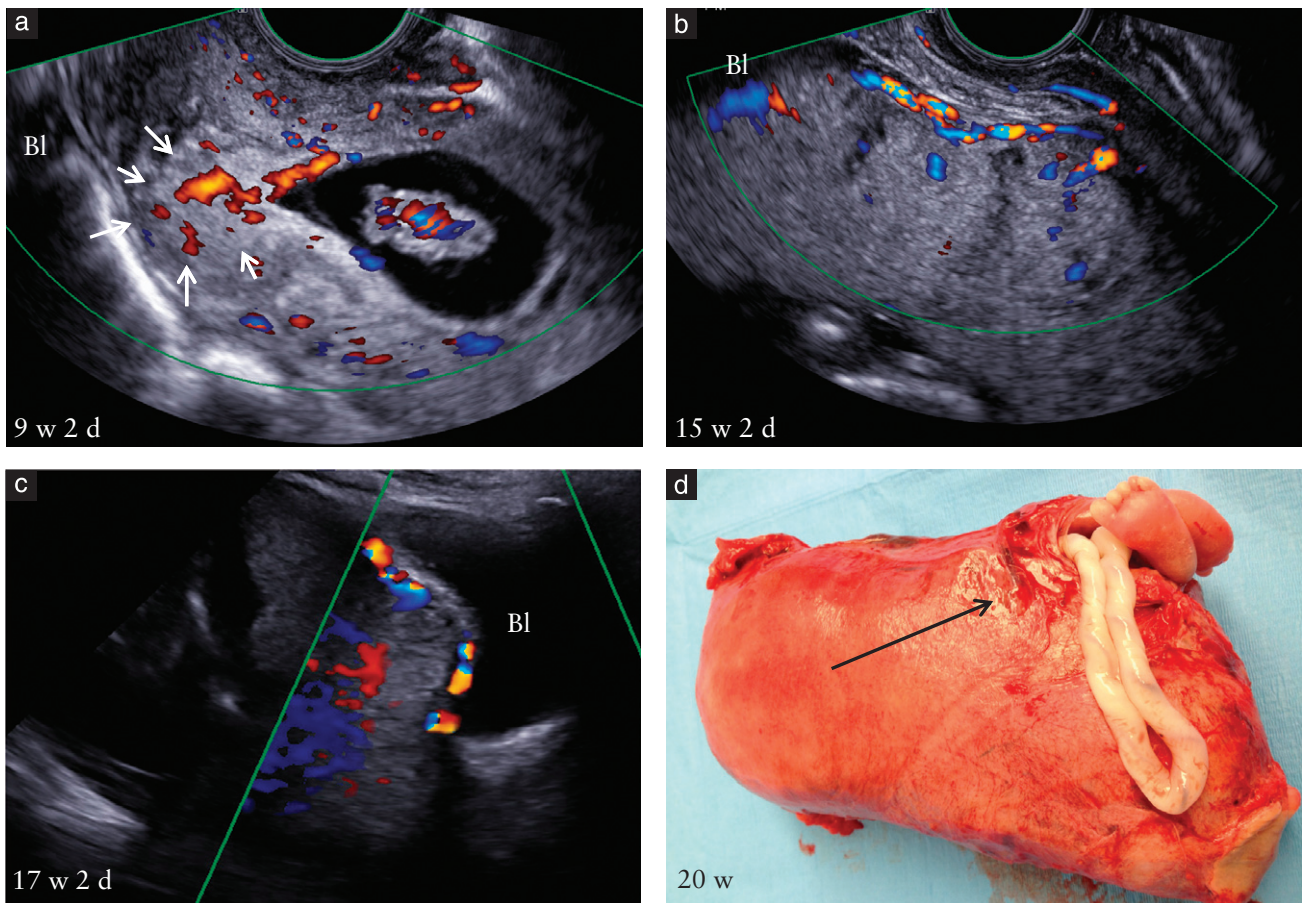


Figure 3 Case 6. (a,b,c) Color Doppler images of Cesarean scar pregnancy in a retroverted uterus at 9+2 weeks (a) (with placental implantation in the niche of the scar indicated (arrows)), and 15+2 weeks (b), and of the morbidly adherent placenta at 17+2 weeks (c). The patient's clinical presentation (intractable bleeding and cervical shortening) at 19 weeks led to hysterectomy at 20 weeks. (d) The excised uterus; placental invasion rendered the anterior lower uterine segment paper thin. During surgery, while handling the uterus, it ruptured, extruding the cord and part of the placenta (arrow). Histology was consistent with percreta. Bl, bladder.

20 weeks. It is important to stress that similar cases with unforeseen emergencies have been described in the literature. In our in-depth review of CSP⁹, we identified 46 articles with 47 cases of MAP in the early second trimester, in which the diagnosis of CSP or MAP was established early in pregnancy. To distinguish these from the 'classical' third-trimester MAP, we used the term 'early placenta accreta' when their description matched the sonographic definition of CSP. All but nine of these 47 patients had previous CD and most of the nine had undergone a prepregnancy intrauterine surgical procedure. Of the 46 articles, 29 were published after the year 2000, reflecting the increasing trend of CSP leading to MAP. Spontaneous uterine rupture was seen in 15 of the 47 pregnancies; most were 'silent', followed by bleeding, shock and hemoperitoneum ending in hysterectomy. UAE to curb bleeding was performed in five of the 47 patients. Thirty-seven had laparotomy, 35 with hysterectomy; one of these had an arteriovenous malformation. In 10 of the 46 reviewed articles, with patients diagnosed with uterine rupture in the first or second trimester, the clinical description was identical to that of early placenta accreta or CSP. From these descriptions, it is evident that the rupture occurred due to and at the site of a CD scar. The obvious clinical

and histological similarities between these cases makes it hard to distinguish particular ones as being typical MAP or typical CSP: compelling support for a hypothesis of their common pathogenesis¹⁹. These cases, as well as similar and previously reported, mostly sporadic, cases, clearly indicate that CSP is a precursor of MAP.

The literature describes pregnancies implanted low and anteriorly as being 'on the scar', termed 'true scar pregnancy', differentiating them from gestations found entirely surrounded by myometrium, and 'in the scar', or in the niche of scar, with a thin or no myometrium between the gestational sac and the bladder^{24,25}. In our Cases 1–3 and Case 5, the sac was clearly on the scar, while in the rest, the implantations were in the niche of the scar. The question as to whether a previous CD scar has to have a defect (niche) for invasive placental penetration to take place may remain unanswered based upon this series. The theory of Kliman *et al.*²⁶, that the trophoblast has a propensity to adhere to denuded scar tissue, may provide some explanation in answer to this question. One thing seems clear: the post CD uterine niche is apparently a risk factor for CSP²⁷. Regardless of the exact site of placental implantation ('on' the scar or 'in' the niche), in a continuing pregnancy the placental

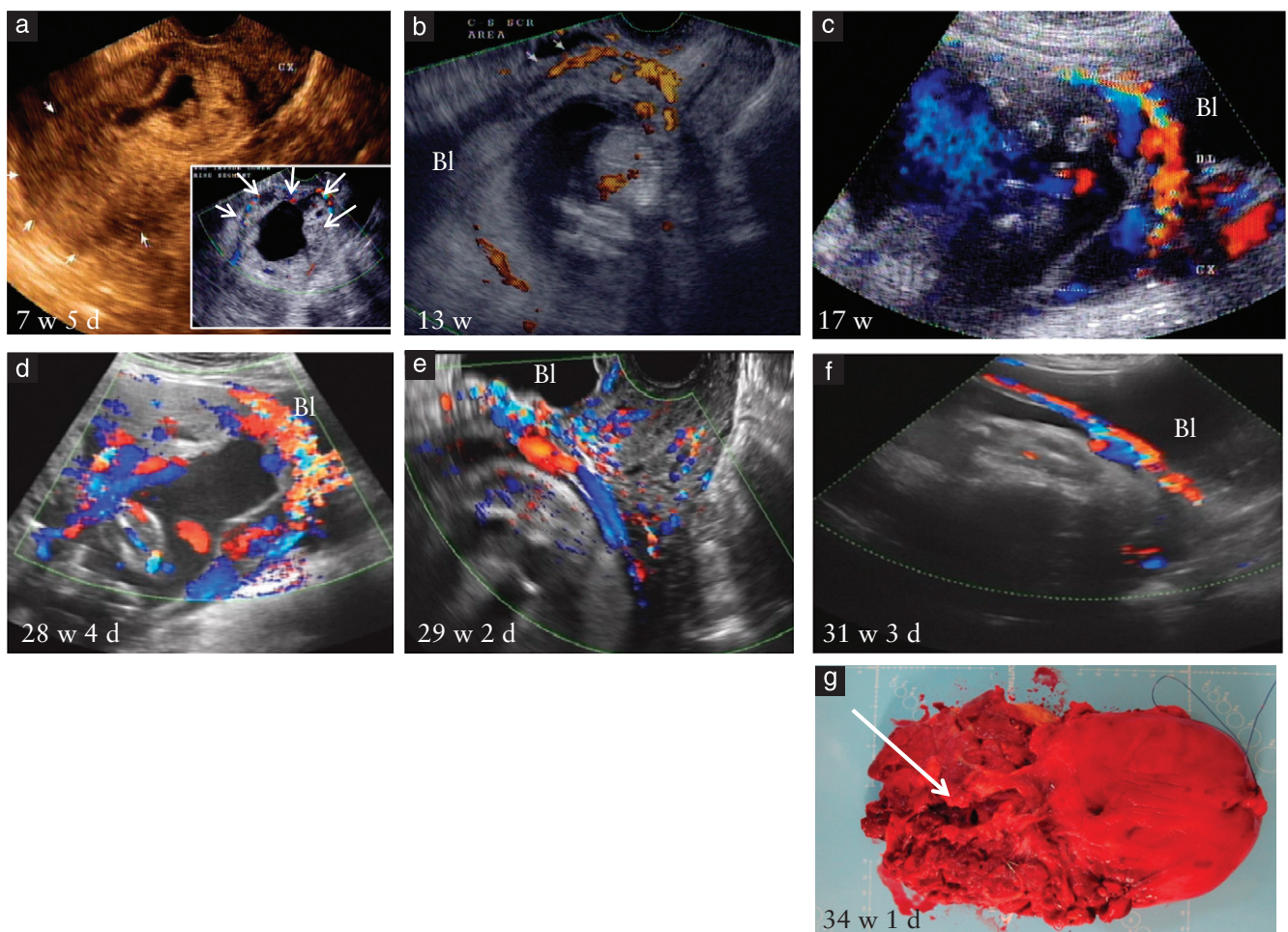


Figure 4 Case 10. Serial gray-scale and color Doppler images of Cesarean scar pregnancy at 7 + 5 weeks (a) (with placental implantation in the niche of the scar indicated by small arrows in the inset image), 13 weeks (b), 17 weeks (c), 28 + 4 weeks (d), 29 + 2 weeks (e) and 31 + 3 weeks (f), demonstrating anterior and low implantation of the placenta, its lacunar nature and its vascularity. (g) The uterus was excised at the time of Cesarean delivery at 34 + 1 weeks; histology was consistent with percreta. Area of placental invasion is indicated (arrow). Bl, bladder.

location and insertion site will remain unchanged, with the placenta firmly 'anchored' in/on the scar and invading the available thin myometrium or scar tissue, penetrating to the level of the uterine serosa or the bladder. Moreover, the distinction between in and on the scar/niche may become irrelevant at around 7–9 weeks, as at this time the gestational/chorionic sac exceeds the size of the niche and 'rolls', at first towards the lower part of the previously empty uterine cavity and later, during the second trimester, progressively into the available space, filling the entire uterine cavity. In our opinion, until more data are available describing the natural history of either kind of placental implantation, the discussion of on or in the scar must be postponed, since management or treatment of this faulty placental implantation is dictated by the evolving clinical picture rather than its initial location.

The current literature²⁸ as well as our observations suggest that there is an unmistakable histological progression through pregnancy, from CSP to MAP; all 10 cases in this series, diagnosed early in pregnancy as CSP, ended with histologically proven placenta percreta at delivery. Furthermore, it has been found that a short time interval between a previous CD and the subsequent conception

may increase the risk for MAP or CSP²⁹, but our small number of cases and lack of a control group does not allow us to comment on this issue. We firmly believe that it is therefore reasonable that every patient who has had a previous CD and presents with an early first-trimester pregnancy should undergo transvaginal ultrasound imaging to ascertain the location of the gestational sac and the site of placental insertion. The feasibility of routine imaging in such cases has been shown^{30,31}, but further clinical proof of its efficacy is required. If an anteriorly attached, low-lying early gestation (with or without heart activity) is identified, it should be considered as a CSP until proved otherwise by ruling out a cervical pregnancy and a miscarriage in progress. If a CSP is diagnosed, the patient can be given the option of terminating or continuing the pregnancy. If the latter is chosen, they should be advised that their chances of achieving the desired delivery (usually premature) of live offspring should be weighed against the significantly high risks of premature delivery, hysterectomy and permanent loss of fertility, and particularly the risks of uterine rupture, massive blood loss, shock and even death.

One final thought . . . our personal impression is that there is very limited awareness in the community of

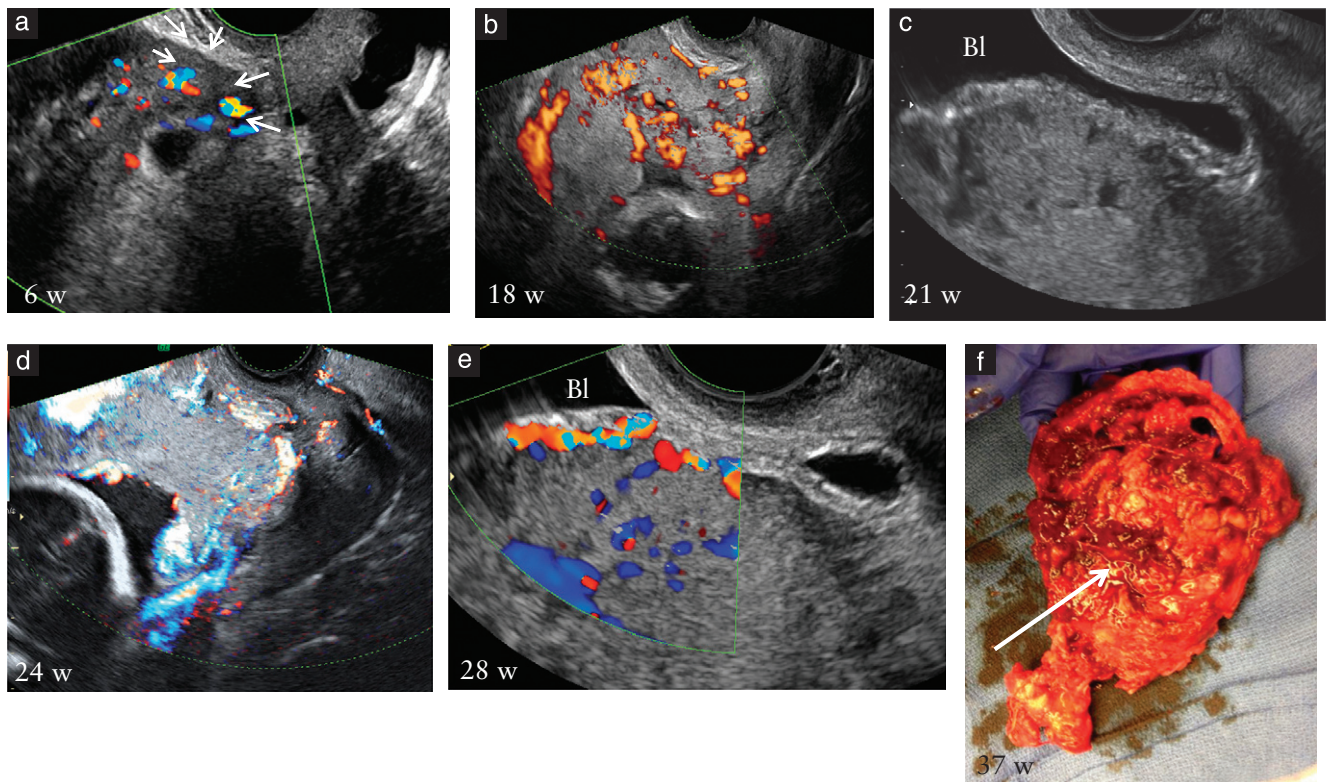


Figure 5 Case 7. Color Doppler imaging depicting features of placental invasion of the uterine wall below the bladder in a Cesarean scar pregnancy at 6 weeks (a) (with placental implantation in the niche of the scar indicated by small arrows) and 18 weeks (b). (c,d,e) Sonographic evidence of the morbidly adherent placenta at 21 weeks (c), 24 weeks (d) and 28 weeks (e). (f) The uterus was excised after Cesarean delivery at 37 weeks; histology was consistent with percreta. The arrow indicates the area of placental invasion. Bl, bladder.

obstetric and gynecological practitioners as to the early and correct identification of CSP. Our Case 9 illustrates this fact. It was only at the second-trimester scan and following an episode of vaginal bleeding that the placental pathology was identified. Reviewing the first-trimester ultrasound images, the diagnosis of CSP was made. It is not known if this patient would have considered intervention in the first trimester. However, it is clear that by not establishing the correct early diagnosis of CSP and informing the patient of its possible consequences, she was denied her management options.

In conclusion, we believe that the cases in this series provide further validation for the hypothesis that, sharing the same histopathology, CSP is the most common of the precursors of MAP.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:



Figure S1 Case 4. Gray-scale ultrasound image of Cesarean scar pregnancy at 8 weeks, with placental implantation in the niche of the scar indicated by small arrows (a), and color Doppler image at 12 + 5 weeks (b). The diagnosis of morbidly adherent placenta was established with color Doppler at 23 + 5 weeks (c) and confirmed at 33 weeks (d). (f) The uterus, excised at 34 weeks, with placental implantation site indicated (long arrow) histology was consistent with percreta. Bl, bladder

Figure S2 Case 9. Gray-scale ultrasound imaging at 8 + 3 weeks (a), 11 + 5 weeks (b) (with placental implantation in the niche of the scar indicated by small arrows) and 15 + 1 weeks (c) attested to a low, anterior placental implantation below the bladder, consistent with Cesarean scar pregnancy. (d,e) At 23 + 5 weeks, the diagnosis of morbidly adherent placenta was made. (f) At 32 weeks uncontrollable uterine contractions led to Cesarean delivery and hysterectomy; the site of placental invasion is indicated (long arrow). Histology was consistent with percreta. Bl, bladder; Cx, cervix.

Figure S3 Case 2. Gray-scale ultrasound image of Cesarean scar pregnancy at 9 + 2 weeks (a), with placental implantation on the scar indicated (small arrows). Color Doppler imaging at 23 weeks (b) and 34 weeks (c) was consistent with a morbidly adherent placenta. (d) The uterus was excised after Cesarean delivery at 36 weeks; the area of placental implantation is indicated (long arrow). Histology was consistent with percreta. Bl, bladder.

Figure S4 Case 3. Gray-scale (a) and color Doppler (b) ultrasound images at 7 + 4 weeks in Cesarean scar pregnancy, with placental implantation on the scar indicated (small arrows). (c) Color Doppler imaging at 22 weeks was consistent with a morbidly adherent placenta. (d) The uterus was excised at 36 weeks, at the time of Cesarean delivery; the area of placental invasion is indicated (long arrow). Histology was consistent with percreta. Bl, bladder.

Figure S5 Case 5. Gray-scale and color Doppler ultrasound images of Cesarean scar pregnancy at 8 + 4 weeks, with site of placental implantation on the scar indicated (a, small arrows), and of the developing morbidly adherent placenta at 16 weeks (b), 26 + 4 weeks (c) and 33 weeks (d). (e) The excised uterus at 34 weeks, with site of placental invasion indicated (long arrow); histology was consistent with percreta. Bl, bladder.