

CLINICAL PRACTICE

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Placenta Accreta Spectrum

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

A 36-year-old woman with three previous cesarean deliveries is referred at 28 weeks of gestation because of placenta previa detected on ultrasonography. Other ultrasonographic findings include multiple intraplacental lacunae and loss of the normal retroplacental hypoechoic zone in the area underlying the dome of the maternal bladder. Placenta accreta is suspected. The course of the patient's pregnancy otherwise has been normal. How should she be counseled and her care be managed?

THE CLINICAL PROBLEM

PLACENTA ACCRETA SPECTRUM IS THE GENERAL TERM APPLIED TO ABNORMAL adherence of the placental trophoblast to the uterine myometrium; it is also referred to as morbidly adherent placenta. The spectrum includes placenta accreta (attachment of the placenta to myometrium without intervening decidua), placenta increta (invasion of the trophoblast into the myometrium), and placenta percreta (invasion through the myometrium, serosa, and into surrounding structures) (Fig. 1). The major clinical problem occurs when the placenta does not detach normally from the uterus after delivery of the fetus, leading to bleeding, which is often severe.

Placenta accreta spectrum is one of the most dangerous conditions associated with pregnancy, because hemorrhage may result in multisystem organ failure, disseminated intravascular coagulation, need for admission to an intensive care unit, hysterectomy, and even death.¹⁻⁵ Outcomes are generally improved with antepartum diagnosis and care by a multidisciplinary team with expertise in the condition.^{6,7} The potential for bleeding correlates with the degree to which the placenta has invaded the myometrium, the area of abnormal adherence involved, and the presence or absence of invasion into extrauterine tissues such as the bladder or parametrial tissues. Morbidity is high; more than half of women receive transfusions of blood products, and a third have incidental cystotomy in association with surgical management.¹⁻³ Ureteral injury, vesicovaginal fistula, and the occurrence of reoperation are less frequent complications.

Placenta accreta spectrum results from the absence of the normal decidua basalis, usually from surgical trauma, such that the trophoblast attaches to or invades the exposed and scarred myometrium. The incidence has increased during the past several decades in association with increasing rates of cesarean delivery. Reports from referral centers suggest that accreta occurred in approximately 1 in 4000 deliveries in the 1970s,⁸ 1 in 2500 deliveries in the 1980s,⁹ and, more recently,

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KEY CLINICAL POINTS

PLACENTA ACCRETA SPECTRUM

- The incidence of placenta accreta spectrum has increased by a factor of approximately 8 since the 1970s, probably owing to increases in cesarean delivery.
- Women with major risk factors, such as placenta previa, previous cesarean delivery, endometrial ablation, or other uterine surgery, should undergo obstetrical sonography in the middle-to-late second trimester to assess for possible placenta accreta spectrum.
- Patients with suspected placenta accreta spectrum should be referred to a center with multidisciplinary expertise and experience.
- Recommended management of suspected placenta accreta spectrum is planned cesarean hysterectomy with the placenta left in situ. However, surgical management may be individualized.
- In most cases, planned preterm delivery at 34 weeks of gestation is recommended to best balance maternal and neonatal risks. Earlier delivery may be warranted in women with labor, bleeding, or other complications.

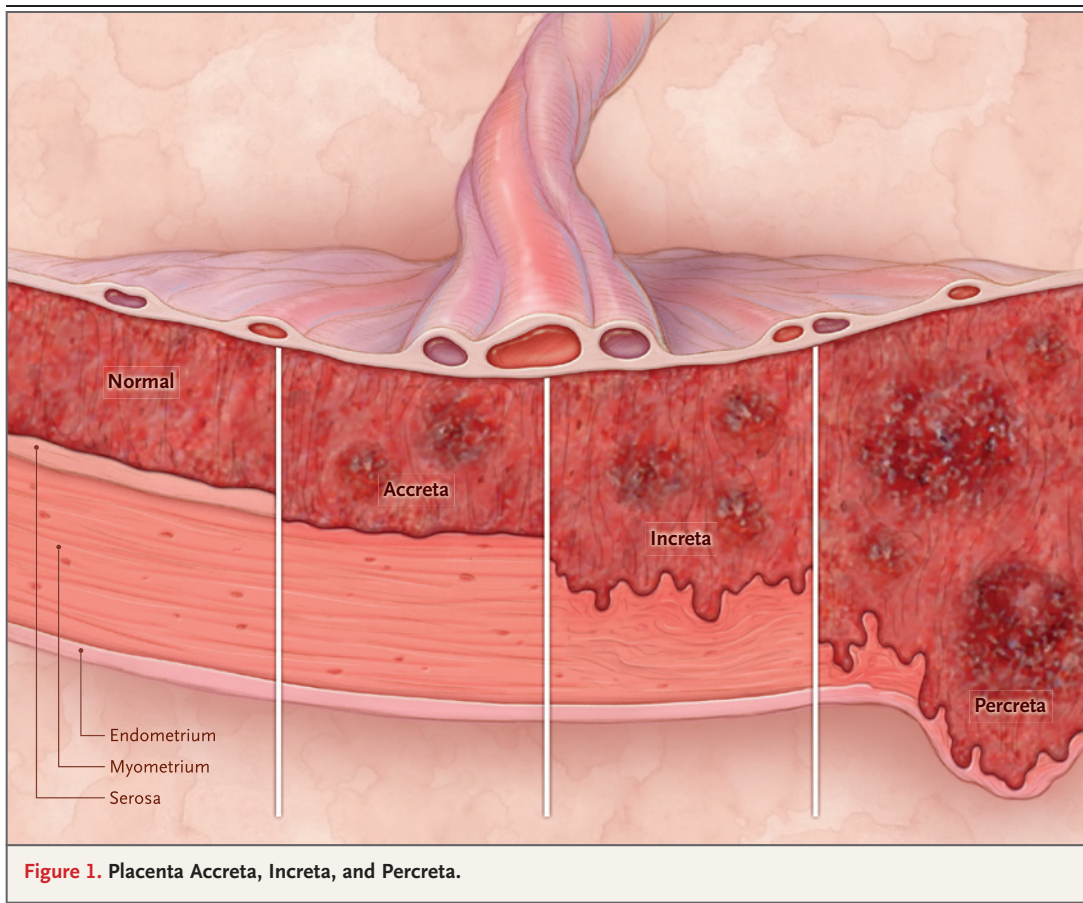


Figure 1. Placenta Accreta, Increta, and Percreta.

1 in 533 to 1 in 730 deliveries.^{5,10} Placenta accreta spectrum is now the most common reason for both hysterectomy associated with cesarean delivery¹¹ and peripartum hysterectomy.¹² It also is a rare but important contributor to maternal mortality in the United States.¹³

RISK FACTORS

Placenta accreta spectrum may occur after any procedure or manipulation that damages the endometrium, including uterine curettage, myomectomy, endometrial ablation, uterine-artery

embolization, or manual removal of the placenta.¹⁴ It has been reported to occur in 2% of pregnancies after hysteroscopic lysis of intrauterine adhesions¹⁵ and in as many as 32% of pregnancies after endometrial resection or ablation.¹⁶ However, the most common risk factors are placenta previa (placenta that partially or completely covers the cervical os) and previous cesarean delivery; the risk is greater when both factors are present and when the previa overlies the scar.⁴ The greater the number of previous cesarean deliveries, the higher the risk.⁴ For example, the risk of accreta with placenta previa among women who have undergone previous cesarean delivery is 11% after one procedure, 40% after two procedures, and 61% after three procedures (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).⁴ Other risk factors include an abnormally adherent placenta in a previous pregnancy, advanced maternal age, increasing parity, and in vitro fertilization.^{17,18}

STRATEGIES AND EVIDENCE

Although placenta accreta spectrum is increasing in frequency, high-quality data to guide management are sparse. Few randomized clinical trials have been conducted, and most information is derived from cohort studies, case series, and expert opinion. Accordingly, clinicians use varied approaches for many aspects of care.

DIAGNOSTIC EVALUATION

Women with major clinical risk factors for placenta accreta spectrum (e.g., placenta previa, previous cesarean delivery, endometrial ablation, or other uterine surgery) should undergo diagnostic evaluation by a practitioner with expertise in this condition.^{1,2,7} Obstetrical sonography in the second or third trimester of pregnancy is the mainstay of antenatal diagnosis, and abnormalities suggestive of placenta accreta spectrum are well described (Fig. 2).^{19,20} The condition is occasionally identified in the first trimester, typically by identification of an ectopic pregnancy in which the embryo is embedded in the myometrium of a previous cesarean-section scar. If such pregnancies are not medically or surgically terminated, they can result in placenta accretas.

Ultrasonography in the second and third trimesters is reported to identify placenta accreta spectrum with sensitivities and specificities of

80 to 90%.^{19,20} These may be overestimates, however, because data are derived from experts aware of the a priori risk on the basis of clinical risk factors. There is considerable interobserver variability in identification of the condition,²¹ and accuracy is markedly lower if clinicians are unaware of clinical information.²²

Magnetic resonance imaging (MRI) also has a sensitivity and specificity of 80 to 90% for the prediction of placenta accreta spectrum.²³ As with ultrasonography, reports probably overestimate accuracy because MRI is performed only

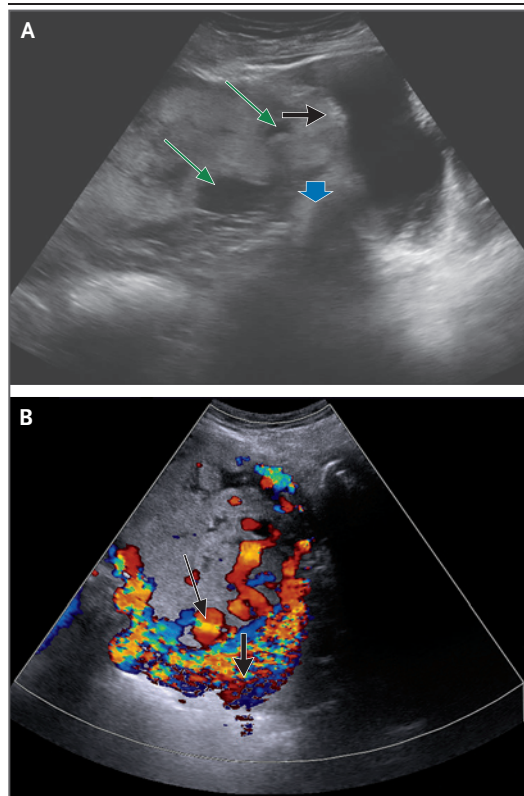


Figure 2. Ultrasonographic Findings and Placenta Accreta Spectrum.

In Panel A, a gray-scale ultrasonographic image shows placenta previa (blue arrow), multiple vascular lacunae (green arrows), and interruption of the uterine serosa-bladder interface (black arrow). Other findings may include loss of the normal hypoechoic retroplacental myometrial zone and extension of the villi into the myometrium or beyond.^{19,20} In Panel B, a color Doppler study shows turbulent flow in lacunae (thin arrow) and increased subplacental vascularity (thick arrow) in the placenta in a case of placenta accreta (arrow). Other findings may include vessels bridging the placenta to the uterine margin and gaps in myometrial blood flow.^{19,20}

when there is a very high a priori risk. MRI is reported to be useful in cases of posterior placenta previa or to assess potential bladder invasion.^{19,23} However, MRI is expensive and requires expertise in the diagnosis of accreta that is not widely available. MRI was not superior to ultrasonography in two small studies directly comparing the two screening methods^{24,25} and has not been shown to improve diagnosis or outcomes as compared with ultrasonography alone.

OBSTETRICAL MANAGEMENT

A major challenge is determining the appropriate timing of delivery to balance the neonatal risks of preterm birth with planned early delivery against the risk of bleeding or labor leading to emergency surgery. Because most patients with placenta accreta spectrum have placenta previa, delaying delivery toward term decreases the risk of prematurity but increases the likelihood of labor and bleeding. A decision analysis involving women with accreta and placenta previa showed that delivery at 34 weeks of gestation was the preferred strategy for balancing maternal and neonatal risks.²⁶ In the absence of better information, planned delivery at 34 weeks of gestation is considered appropriate in asymptomatic women in whom clinical and imaging findings strongly suggest placenta accreta spectrum. There is an increased risk of emergency delivery in women with previous preterm birth, bleeding, and contractions; thus, delivery before 34 weeks of gestation may be prudent in cases of bleeding or suspected labor. Delivery may reasonably be delayed to 35 or 36 weeks in asymptomatic patients with placenta previa in whom clinical and imaging findings suggest a low risk of placenta accreta spectrum.

As with all cases of planned preterm birth, glucocorticoids should be administered to the mother (12 mg of betamethasone given intramuscularly at 2 to 7 days before delivery and repeated once 24 hours later) to enhance fetal pulmonary lung maturity.²⁷ Avoiding intercourse and cervical examinations are of unproven efficacy, although these measures make intuitive sense in women with placenta previa. Bed rest is also recommended in women with bleeding, although it is not known whether it affects outcomes. Most centers only hospitalize women with bleeding or threatened labor, but some admit all women with the condition in the middle

of the third trimester. Factors such as whether the woman has assistance at home and the distance from the hospital may influence the decision whether to hospitalize.

Women with suspected placenta accreta spectrum should deliver in a center with appropriate expertise and experience.²⁸ Delivery in such centers has been associated with lower rates of hemorrhage and other complications than with standard care.^{6,7,12} Multidisciplinary expertise may include maternal–fetal medicine, gynecologic surgery, gynecologic oncology, anesthesia, transfusion medicine, interventional radiology, trauma and vascular surgery, and urology and the presence of intensivists, neonatologists, and specialized nursing staff. It is critical that the blood bank is capable of massive transfusion with multiple types of blood products. The use of an antenatal or preoperative checklist, team training, and simulation are advised, although efficacy has not been proved.^{7,28} Depending on distance, transfer of women who receive a diagnosis of placenta accreta spectrum at the time of laparotomy (Fig. 3) to such a center should be considered if hysterotomy or hysterectomy can be safely delayed.²⁸

DELIVERY

The preferred surgical approach to placenta accreta spectrum remains uncertain, although most studies show improved outcomes with planned cesarean hysterectomy before the onset of labor or bleeding.^{1,2,29} The surgery should be performed in a well-equipped operating suite with experienced ancillary personnel, and the anesthesiology team must be familiar with managing the care of obstetrical patients in the context of severe hemorrhage.

The preferred anesthesia for delivery is also uncertain. In cases of severe hemorrhage, it is safest to use general anesthesia with endotracheal intubation. However, continuous lumbar epidural and spinal anesthesia have been used with excellent outcomes in women with placenta accreta spectrum.³⁰ Conversion from regional to general anesthesia if hemorrhage occurs is another reasonable approach.

Cross-matched blood products sufficient for massive hemorrhage should be in the operating suite before surgery begins. Other steps to ensure proper care of obstetrical hemorrhage should be used, including point-of-care testing for blood

counts and clotting status, the use of rapid-infusion equipment, red-cell salvage (Cell Saver), and blood and patient warming. Use of a massive-transfusion protocol is encouraged.³¹ Specific replacement protocols have not been assessed in women with placenta accreta spectrum. However, a trial involving trauma patients with severe hemorrhage compared administration of plasma, platelets, and red blood cells in a 1:1:1 ratio with their administration in a 1:1:2 ratio. There was no significant between-group difference in the primary outcomes of overall mortality at 24 hours or at 30 days, but the 1:1:1 ratio resulted in a lower rate of death due to hemorrhage in the first 24 hours.³² In another randomized trial involving women with postpartum hemorrhage (9% of whom had placenta accreta or previa), administration of tranexamic acid was associated with a lower rate of death due to bleeding than placebo.³³

Large-bore venous access and pneumatic compression devices are recommended, and central venous access should be considered. One retrospective cohort study showed decreased ureteral injury after ureteral stent placement before hysterectomy,¹ although routine use is of uncertain efficacy. Either a midline abdominal incision or Cherney incision (transverse incision with transection of the rectus muscles at their insertion on the pubic symphysis) allows exteriorization of the uterus and adequate access to the pelvic sidewalls. Once the abdomen is open, the gravid uterus is exteriorized so that the fetus is delivered through an incision (usually fundal) that avoids disrupting the placenta (identified by sonography before or during the procedure). The placenta and attached secured segment of umbilical cord are left in situ; retrospective series indicate markedly less blood loss when there is no attempt at placental removal in cases with a high suspicion of accreta.^{1,2} The hysterotomy is expeditiously closed with a running locked suture. Modified surgical approaches to hysterectomy are also used; discussion of these is beyond the scope of the present article.³⁴

Placental removal may be considered in patients with a low risk of placenta accreta who strongly wish to maintain fertility (e.g., a woman with an anterior placenta previa with one previous cesarean delivery and no sonographic evidence of accreta). The cesarean section should be performed with the same preparation and in

the same location as other cases (perhaps at 36 weeks of gestation) with a hysterotomy that avoids the placenta. If the placenta does not easily separate from the uterus, or if there is bleeding, hysterectomy should be undertaken.

Women with placenta accreta have an increased risk of postpartum venous thromboembolism, owing largely to their complex surgical deliveries, often with associated immobilization. Although studies are lacking to inform benefits and risks, it is reasonable to consider postpartum thromboprophylaxis in these women.

AREAS OF UNCERTAINTY

There is uncertainty regarding the role of routine pelvic devascularization, which typically involves preoperative placement of internal iliac balloon catheters that are inflated after delivery of the baby. Some observational studies suggest that balloon placement is associated with reduced

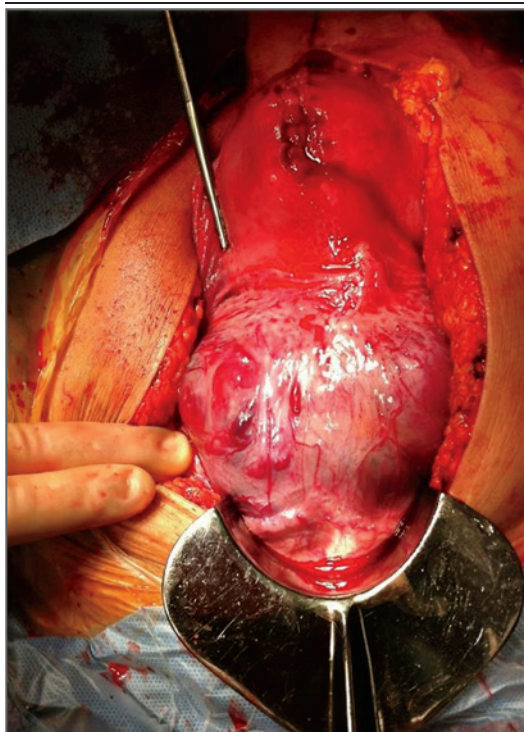


Figure 3. Uterus with Placenta Percreta Visible at the Time of Laparotomy.

The placenta is bulging through the lower uterine segment, and there is evidence of increased vascularity. The fetus has been delivered through a fundal uterine incision, which has been repaired.

blood loss,^{35,36} especially in cases of percreta.³⁶ However, other studies have shown no benefit,^{37,38} and complications such as arterial damage, infection, and occlusion have been described.³⁹ One small randomized trial involving 27 women showed no significant difference in bleeding between women who received balloon catheters and those who did not.⁴⁰

A major uncertainty relates to “conservative management” of placenta accreta spectrum intended to preserve the uterus for future pregnancy or to avoid surgical complications. The most common procedure is to perform a planned laparotomy and hysterotomy (avoiding the placenta) with delivery of the baby. The umbilical cord is ligated close to the placenta, the uterine incision is closed, and the uterus is left in situ. It is expected that the placenta will reabsorb over time. In many cases, pelvic devascularization with embolization is used after cesarean delivery. Although methotrexate has been used in conservative management, its use is not recommended, given the lack of evidence of efficacy and the potential risks.

In a case series from France involving 167 women with suspected placenta accreta who received conservative treatment, 78% avoided hysterectomy,⁴¹ and several patients so treated have had subsequent successful pregnancies.⁴² However, in the French cohort, nearly a quarter of the patients underwent hysterectomy at the time of or within 6 weeks after the cesarean section, mostly owing to hemorrhage; serious complications occurred in 6%, and there was one death.⁴¹ In addition, it is uncertain whether all these women truly had placenta accreta spectrum, given the absence of a hysterectomy specimen for histologic confirmation of the diagnosis. The women who received conservative treatment in this study had considerably fewer risk factors for accreta, such as previous cesarean delivery, placenta previa, and sonographic evidence of accreta, than those included in other series. Serious complications also have been noted in other studies with conservative management, owing to delayed and unpredictable hemorrhage and infection.⁴³ Accordingly, women should be counseled regarding the risks of conservative management; randomized trials are needed to define the benefits and risks of this approach.

Another controversial strategy is planned delayed hysterectomy. Delivery without disrupting

the placenta is performed as above, followed typically by a period of pelvic devascularization and expectant care (for days to weeks) to allow partial involution of the placenta and decreased uteroplacental blood flow. In theory, this allows for a hysterectomy with fewer complications and has been proposed as most beneficial in particularly problematic cases, such as definite placenta percreta.⁴⁴ A retrospective series of 21 cases suggested better outcomes with delayed hysterectomy (6 weeks after delivery) than with immediate hysterectomy.⁴⁵ However, this approach involves two separate major surgeries, and the delay poses a risk of infection and spontaneous bleeding that may require emergency surgery.

Partial resection of areas of “focal” placenta accreta or the entire lower uterine segment with hemostatic closure of the myometrial defect has also been proposed.^{46,47} However, it is challenging to predict focal accreta with accuracy, data are insufficient to inform efficacy, and the chance of subsequent pregnancy is low.

Although several biomarkers (e.g., elevated levels of maternal serum alpha fetoprotein,⁴⁸ placental pregnancy-associated plasma protein A,⁴⁸ and pro-brain natriuretic peptide⁴⁹) have been associated with placenta accreta spectrum, none have proven usefulness for clinical prediction. New imaging methods, such as three-dimensional power Doppler, may improve the accuracy of diagnosis and are under investigation.

GUIDELINES

Owing to a lack of high-quality evidence, few guidelines exist for the management of placenta accreta spectrum. Nonetheless, opinions have been published by relevant professional organizations in the United States.^{3,50} Our recommendations are consistent with other published recommendations (summarized in Table 1).

CONCLUSIONS AND RECOMMENDATIONS

The woman described in the vignette has suspected placenta accreta spectrum in the context of major risk factors, including placenta previa and previous cesarean delivery. Women with placenta accreta spectrum are at substantial risk for serious complications related to hemorrhage and surgery (cesarean delivery and commonly

Table 1. Guidelines for Placenta Accreta Spectrum.***Antepartum**

Women with risk factors for placenta accreta spectrum (e.g., placenta previa, previous cesarean delivery, endometrial ablation, or other uterine surgery) should undergo targeted obstetrical ultrasonography in the middle-to-late second trimester to assess for suggestive findings.

Preoperative counseling should include discussion of the risks posed by placenta accreta spectrum, including the potential for massive hemorrhage, complications of surgery, and hysterectomy.

Although planned delivery is desirable, a contingency plan should be in place in case emergency delivery is indicated.

Antenatal glucocorticoids should be administered to the mother (12 mg of betamethasone given intramuscularly at 2 to 7 days before delivery and repeated once 24 hours later) to enhance fetal pulmonary maturity.

Delivery

Delivery should occur in a center with a multidisciplinary team experienced in the care of the condition and a blood bank with the capacity for massive transfusion.

Outcomes are improved with scheduled delivery before the onset of labor or bleeding. In most cases, planned preterm delivery at 34 weeks of gestation appears to best balance maternal and neonatal risks. Amniocentesis to assess fetal pulmonary maturity is not required.

The generally recommended management of placenta accreta spectrum is planned cesarean hysterectomy with a hysterotomy that avoids the placenta, which is left in situ. Individualized, alternative management strategies may be used after appropriate counseling.

In the context of intraoperative hemorrhage, key measures include aggressive volume expansion, transfusion of blood products, and correction of coagulation.

* The guidelines are adapted from recommendations of the Society for Maternal–Fetal Medicine³ and the American College of Obstetricians and Gynecologists.⁵⁰

hysterectomy). Women with risk factors including placenta previa, previous cesarean delivery, endometrial ablation, or other uterine surgery should undergo ultrasonography in the middle-to-late second trimester to screen for the condition. Antenatal diagnosis allows for planned delivery and, if indicated, referral to a center with an experienced multidisciplinary team; care in such centers has been associated with better

outcomes. She should be counseled that standard management is planned cesarean hysterectomy with delivery at 34 weeks of gestation. Delivery earlier in gestation may be appropriate in the context of bleeding or labor.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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