

Case Scenario: Perioperative Management of a Multigravida at 34-week Gestation Diagnosed with Abnormal Placentation

Elena Reitman, M.D.,* Patricia C. Devine, C.M.D.,† Sherelle Lea Laifer-Narin, M.D.,‡
Pamela Flood, M.D.§

PERIPARTUM hemorrhage is responsible for 150,000 maternal deaths worldwide each year.¹ Although the risk of maternal death has decreased over the preceding century, there has recently been a concerning suggestion of an increase in the overall incidence of hemorrhage. Despite multiple advances in medical and surgical care, a steady rise in hemorrhage has been noted within the developed world.¹ Statistically significant increases in the incidence of maternal hemorrhage have been reported in retrospective studies in Canada (from 4.1% to 5.1%) and Australia (from 4.9% to 6.3%).² Similarly, there was an increase in maternal deaths secondary to hemorrhage in the United Kingdom during the years 2000–2002.³ This new uptick in the rate of peripartum hemorrhage has been attributed to increasing maternal age, multiple gestations, and the rise in the rate of cesarean

sections. The most common cause of postpartum hemorrhage remains uterine atony. Disorders of placentation can be associated with either uterine atony or retained placenta. Importantly, in the developed world abnormal placentation is commonly diagnosed before delivery; with proper medical management and multidisciplinary planning, the associated morbidity and mortality can be minimized.

During the past decade the rate of cesarean section has increased for multiple reasons, including an increase in maternal age, *in vitro* fertilization, multiple gestation, a decrease in vaginal breech delivery,⁴ and less frequent vaginal birth after cesarean section. A systematic review of 30 studies from 1997–2002 showed that nearly 90% of women chose to have a cesarean section after a previous cesarean section despite recent evidence for increased neonatal mortality.⁵ Repeated cesarean sections are a risk factor for abnormal placentation.

Diagnosis of placenta previa is an indication of abnormal placentation. It is associated with an increased risk of postpartum hemorrhage due to inability of the lower uterine segment site of placental implantation to contract after placental delivery. In patients with placenta previa who have had previous cesarean delivery, each surgery is associated with an increased risk of placenta accreta. Placenta accreta, an abnormally deep attachment of the placenta into the endometrium and myometrium (the middle layer of the uterine wall), complicates 3% of primary, 11% of secondary, 40% of tertiary, 61% of quaternary, and 67% of higher-order cesarean sections for placenta previa.⁶

In this case scenario, a patient with suspected placenta accreta who required cesarean hysterectomy is presented. The risks and benefits of various anesthetic treatments and transfusion strategies are discussed with a multidisciplinary approach to delivery.

Preoperative Clinical Information

The patient was a 32-yr-old woman at 34 weeks' gestation of her third pregnancy who presented from an outside hospital and had a history of intermittent vaginal bleeding. The patient had a prenatal diagnosis of placenta previa, detected

* Obstetrics Anesthesia Fellow, Department of Anesthesiology, Obstetrical Division, Columbia University, New York, New York. † Assistant Clinical Professor, Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Columbia University. ‡ Associate Professor of Clinical Radiology, Department of Radiology, Division of Ultrasound, Columbia University. § Professor of Clinical Anesthesiology, Department of Anesthesiology, Division of Obstetrical Anesthesiology, Columbia University.

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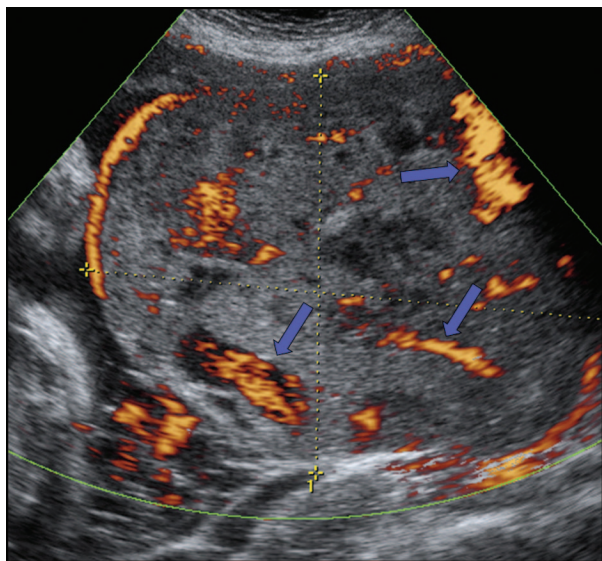


Fig. 1. Ultrasound view of placenta. Highly vascular placenta with prevalent placental lacunae is shown (blue arrows).

during an ultrasound examination at 22 weeks' gestation. Her prenatal course was significant for multiple episodes of vaginal bleeding, one of which had required transfusion with two units of packed red blood cells (pRBCs). Ultrasound examination revealed the presence of multiple lacunar spaces that were concerning for placenta accreta (fig. 1), which led to the patient's transfer to our institution. On admission, the patient was hemodynamically stable with no active bleeding and the fetal heart rate tracing was category 1, indicating a normal fetal heart rate with no intervention required. The patient was of average height and weight and had no pertinent medical history. Her airway was Mallampati class 1. She had undergone a cesarean section for nonreassuring fetal heart rate tracing 3 yr ago and had an uncomplicated repeat cesarean section 14 months before the current presentation, both with neuraxial anesthesia. The patient's hematocrit level was 30%, and all other laboratory values were within normal limits. Because the patient's condition was stable, the obstetricians requested magnetic resonance imaging (MRI) of the placental bed to confirm the degree of placental invasion. MRI using T2-weighted images demonstrated bulging of the lower uterine segment over the bladder, a heterogeneous placenta, and placental lacunae (fig. 2); these findings were suggestive of placenta accreta.

Basic Science Note

Placenta accreta refers to abnormal attachment of the placental villi through the endometrium, directly into the myometrium, whereas placenta increta entails deeper invasion into the myometrium and placenta percreta indicates growth through the serosa with potential for vascular invasion into other organs and structures (fig. 3). The most common risk factor for abnormal placentation is previous cesarean section, but any invasive procedure that

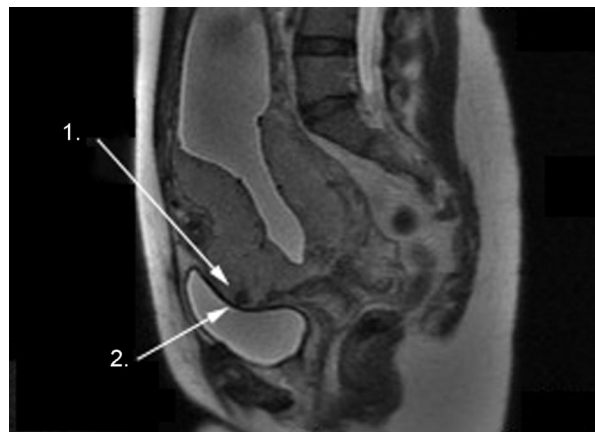


Fig. 2. MRI view of pregnant uterus with placenta accreta. Note heterogeneous placenta with lacunae (1). Placenta bulges into upper bladder surface (2).

might affect the endometrium (including curettage, hysteroscopic surgery, myomectomy, and endometrial ablation) can increase the risk.⁷ Advanced maternal age is also thought to be an independent risk factor, although the lifetime incidence of unreported intrauterine trauma or infection might be an associated risk.⁸ The molecular etiology of abnormal placental invasion is unknown, although it is likely to be due to a defect in the decidua basalis. Histologically, abnormal placentation has been attributed to an absence of the Nitabuch layer, which is thought to represent a boundary for trophoblastic invasion. Differences in oxygen tension in abnormal placental beds have been invoked as a cause of abnormal placental invasion. It has been reported that preferential implantation of embryos into a relatively avascular scar tissue occurs because of decreased oxygen tension.⁹ Deeper invasion in the setting of placenta increta and percreta might result from partial dehiscence of the existing scar.¹⁰

Abnormal placentation might also be due to an unusually extensive trophoblastic invasion. The trophoblastic cells that invade the endometrium are mononuclear cells. Mononuclear cells later fuse to form multinuclear giant

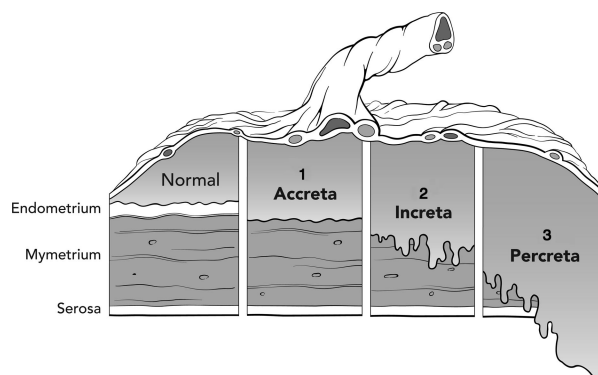


Fig. 3. Diagram of degrees of abnormal placental infiltration. (1) Placenta accreta is adherent to the myometrium. (2) Placenta increta invades the myometrium. (3) Placenta percreta extends beyond the uterine serosa and may invade any other organ.

cells, which are thought to be in a terminal stage of differentiation. In cases of abnormal placentation, the placental junction has few giant cells, potentially representing an abnormally aggressive placenta.¹¹ It is not known to what degree the environment of an old scar or factors intrinsic to the placenta itself predispose to the development of placenta accreta.

Diagnosis

Abnormal placentation is routinely diagnosed on second-trimester ultrasound, but the degree of invasion is more difficult to ascertain. Classic findings on ultrasound are concomitant previa or anterior placenta overlying scar tissue, numerous vascular lacunae, absence of the hypoechogenic layer that represents the normal interface between the placenta and underlying myometrium, absent lower uterine segment between the bladder and placenta, and turbulent or complicated blood flow at the uteroplacental interface. In a retrospective review of the clinical experience and pathology of 12 patients with potential abnormal placentation identified by the preceding criteria, 2 had no adherent placenta on cesarean section, 8 had placenta accreta, 1 had placenta increta, and 1 had placenta percreta. The 10 patients with adherent placentas had a cesarean hysterectomy requiring an average transfusion of five units pRBCs.¹² Transfusion requirements for patients with placenta percreta can be more extensive than for placenta accreta because in placenta percreta, the placental beds that remain after hysterectomy are not constricted by contractile tissue and often continue to bleed.

Ultrasound imaging is very sensitive, if not perfectly specific, for the identification of abnormal placentation, but the degree of uterine invasion is more difficult to visualize because the difference between a placenta accreta and percreta can be measured in millimeters. The only applicable imaging technology with this degree of resolution is MRI.¹³ The most useful indicators of accreta upon nonenhanced MRI are dark intraplacental bands, heterogeneous signal intensity in the placenta, focal areas of uterine bulging, and loss of the interface with adjacent organs. The data available suggest that diagnostic ultrasound has no adverse effects on embryogenesis or fetal growth. In addition, ultrasound scanning has no long-term effects on fetal cognitive function, vision, or hearing. However, color, power, and pulsed Doppler procedures should be performed with caution because of possible adverse thermal effects.¹⁴ There have been no reported delayed adverse sequelae secondary to standard MRI examinations, and the potential risks are considered extremely small or nonexistent. Gadolinium-based contrast material is generally avoided in pregnant women because contrast materials will cross the placenta, appear in the fetal bladder after intravenous administration, and be excreted into amniotic fluid where it may be subsequently swallowed by the fetus.¹⁵

Biomarkers might be useful in identifying patients with abnormal placentation to more accurately identify the degree of uterine invasion. Placental messenger RNA can be detected in maternal blood in the setting of placenta percreta and might be useful as a biomarker for serosal invasion. In a study of 28 women with placenta accreta and 9,321 control subjects, mean gravidity and maternal serum levels of α -fetoprotein and free β human chorionic gonadotropin hormone were significantly higher in women with placenta accreta.¹⁶ The sensitivity and specificity of these biomarkers used individually or together to predict high-grade invasion await prospective study.

Obstetric Management

The obstetric management of expected abnormal placentation usually involves planned cesarean hysterectomy. Although the optimal timing for delivery is uncertain, early delivery is often recommended to minimize additional risks that are associated with emergent surgery. Delivery planning should include the presence of additional surgeons, including a pelvic surgery specialist, and the appropriate instruments enabling a rapid hysterectomy if necessary. As the rate of abnormal placentation continues to increase, it is important to encourage a multidisciplinary approach. Transcatheter arterial embolization for the control of obstetric hemorrhage has been shown to reduce blood loss and avoid hysterectomy in some cases.¹⁷ However, vascular injury has also been reported as a result of this technique. Adequate blood products should be immediately available for transfusion with a rapid infuser. Evidence is now in favor of cell salvage in obstetrics, although this finding remains controversial.¹⁸ Recent evidence indicates that preoperative placement of ureteral stents is also associated with improved clinical outcome because clear identification of the ureters allows rapid completion of the hysterectomy.¹⁹ A vertical midline incision may be considered to achieve optimal visualization. Attempts should be made to avoid disruption of the placenta both during completion of the hysterotomy and delivery of the fetus. To avoid the excessive bleeding that can occur at the time of placenta delivery in these cases, hysterectomy is often initiated immediately after delivery of the fetus without an attempt at placenta removal.

More conservative measures have been described in an attempt to avoid extensive surgery and possibly preserve maternal fertility. Limited data are available regarding conservative management of placenta accreta. In one series from France, the authors report 78% success at uterine preservation leaving the placenta *in situ* and waiting for spontaneous reabsorption.²⁰ However, there are significant risks to conservative therapy. One woman in their series died of immunosuppression and nephrotoxicity related to methotrexate, which was given to induce reabsorption of the placenta.²⁰ Additional reported complications include sepsis, disseminated intravascular coagulation, severe hemorrhage, and de-

layed need for hysterectomy in an emergent setting due to severe hemorrhage.

Anesthesia Management

Most patients who present for routine planned cesarean sections are anesthetized using neuraxial techniques because of concern for the maternal airway. Use of neuraxial anesthesia has the added benefit of preempting the need to resuscitate an anesthetized newborn. This is particularly relevant in the setting of surgery for placenta accreta because the interval from incision to delivery is likely to be prolonged, and the fetus will have time to develop equilibrium concentrations of the maternal anesthetic. Despite these concerns, many planned cesarean sections for placenta accreta are done with general anesthesia because of concerns for hemodynamic instability and the potential requirement for massive transfusion. However, in a classic study of cesarean hysterectomy at five institutions from the 1980s, 32% of planned cesarean hysterectomies were performed under regional anesthesia. There was no difference in intraoperative blood loss or hypotension, and no one required induction of general anesthesia.²¹

The risk-benefit ratio for anesthetic choice in the setting of cesarean hysterectomy is heavily weighted by the likelihood of massive blood loss. In the setting of placenta accreta and increta, surgical clamping of the uterine blood supply after delivery is very effective at controlling blood loss. Case series heavily populated by placenta accreta often document transfusion requirements of four to six units of pRBCs.²¹ However, in placenta percreta, the placental bed may be fed by extrauterine blood supply and these cases are associated with much larger transfusion requirements. If regional anesthesia is chosen, it is important to counsel the patient and her family about the possibility of conversion to general anesthesia in the setting of massive hemorrhage. This approach should only be considered in the setting of a favorable patient airway examination. An unfavorable airway examination might encourage the practitioner to secure the airway from the beginning of surgery with any advanced techniques that are necessary.

Recommendations for Transfusion

Massive blood loss is defined as the loss of more than half of blood volume in 3 h or ongoing loss of more than 150 ml/min. Experience with massive transfusion in the setting of trauma has shown an improved outcome by using a 1:1:1 ratio of packed red blood cells, fresh frozen plasma, and platelets.²² Red blood cell transfusion is required when 30–40% of the blood volume is lost in the setting of crystalloid replacement and a normal starting hematocrit level. However, many pregnant women are naturally anemic due to a greater increase in plasma volume than erythrocyte volume. Consequently, hemoglobin level decreases by approximately 10%.²³ Recombinant factor VIIa has been considered a “universal pancoagulant.” Recently, Ahonen and Jokela de-

scribed the possible beneficial role of recombinant factor VIIa in the treatment of life-threatening postpartum hemorrhage.²⁴ Its use is supported by level IV and V evidence and is recommended by the European Society of Anesthesiology.²⁵ However, it should not be considered as a substitute for nor should it delay the performance of a life-saving procedure such as embolization or surgery, nor the transfer to a referring center. Tranexamic acid has been studied after routine cesarean section²⁶ and could be considered for prophylaxis after cord clamp. Normally this drug is dosed as a bolus followed by an infusion to maintain steady-state kinetics. No procoagulant factor can be successful in the setting of inadequately addressed surgical bleeding. Additional clinical trials are needed to establish the cost-benefit and risk-benefit profiles for procoagulant drugs and to establish standards for treatment of massive bleeding in pregnancy.

Uterotonic agents should be used in the interval between delivery and hysterectomy. It is common practice to begin an infusion of oxytocin after the delivery of the placenta. Methylergonovine or ergonovine maleate may be administered intramuscularly. Rectal administration of misoprostol was also described for treatment of severe postpartum hemorrhage. It is important to maintain normothermia by aggressively warming blood products and fluids and to treat hypocalcemia to favor normal hemostasis.

Surgical Course

The patient was offered regional anesthesia with the understanding that tracheal intubation would be required during the surgery if bleeding was severe. The patient was given combined spinal-epidural anesthesia with 12 mg bupivacaine, 20 μ g fentanyl, and 200 μ g morphine in the intrathecal space. The epidural catheter was not tested before surgery, but there was no cerebral spinal fluid or blood on aspiration of the catheter. The catheter was dosed once 45 min after spinal placement with 100 mg lidocaine in a 5-ml volume.

The uterine arteries were dissected by the surgeons to allow for immediate cross-clamping after delivery. The uterine dissection was difficult with significant anterior adhesions. The hysterotomy incision was made at the fundus to avoid placental disruption. The fetus was delivered 34 min after skin incision. Apgar scores were 8 and 9. Given the clinical evidence for abnormal placental invasion, the decision was made to proceed with hysterectomy. Attempts to remove the placenta were avoided to minimize bleeding. The uterine incision was rapidly closed with the placenta *in situ*. The hysterectomy was completed in an expeditious manner without complication. Oxytocin infusion was initiated after fetal delivery and maintained until the hysterectomy was completed. A small amount of fluid oozed from the uterine incision site until the specimen was removed. The patient's hematologic values were monitored with point-of-care testing. When the patient's hematocrit level decreased to 22%, transfusion was begun. The pa-

tient received three units pRBCs and 2 l of crystalloid fluids during surgery. She was also given 1 mg midazolam for mild anxiety after delivery. Intubation was not required. The patient and her infant were discharged from the hospital on the fourth postoperative day.

Cesarean hysterectomy is the definitive treatment for uncontrollable hemorrhage; however, over the past two decades more conservative measures have been reported. Pelvic arterial embolization and local tamponade may also play a key role in the management of obstetric hemorrhage. Interventional radiology offers a minimally invasive, fertility-preserving alternative to conventional surgical treatment.²⁷ Either regional or general anesthesia is acceptable depending on the anticipated risk of massive hemorrhage. If massive hemorrhage occurs, it should be treated with a 1:1:1 transfusion ratio of pRBC, fresh frozen plasma, and platelets. Procoagulant factors and drugs have been used successfully to treat massive bleeding after cesarean hysterectomy but should be reserved due to concerns for systemic vascular thrombosis.

Knowledge Gap

Although uterine scarring is clearly a risk factor for the development of abnormal placentation, it is unknown why some placentas become invasive and others do not. Current modalities (history, ultrasound, and MRI) used for diagnosis of abnormal placentation are reasonably sensitive but not very specific. Unfortunately, the treatment, preparation, and monitoring of a patient with suspected abnormal placentation has its own potential side effects that may lead to maternal morbidity in the setting of false diagnosis. As such, better diagnostic tools and biomarkers are needed to improve diagnostic accuracy.

Guidelines for massive transfusion have been developed in the trauma setting but have not been validated in the setting of pregnancy. The recommendation for transfusion of pRBCs and plasma in a 1:1 ratio has been adopted but not properly studied in this setting. Rapid transfusion of a larger percentage of plasma may lead to unexpectedly rapid development of hypocalcemia because plasma has a higher citrate concentration than pRBCs. Consensus guidelines on modern transfusion practices specific to the pregnant woman would provide guidance to practitioners and blood banks and may reduce the still considerable maternal morbidity and mortality in the face of obstetric hemorrhage.

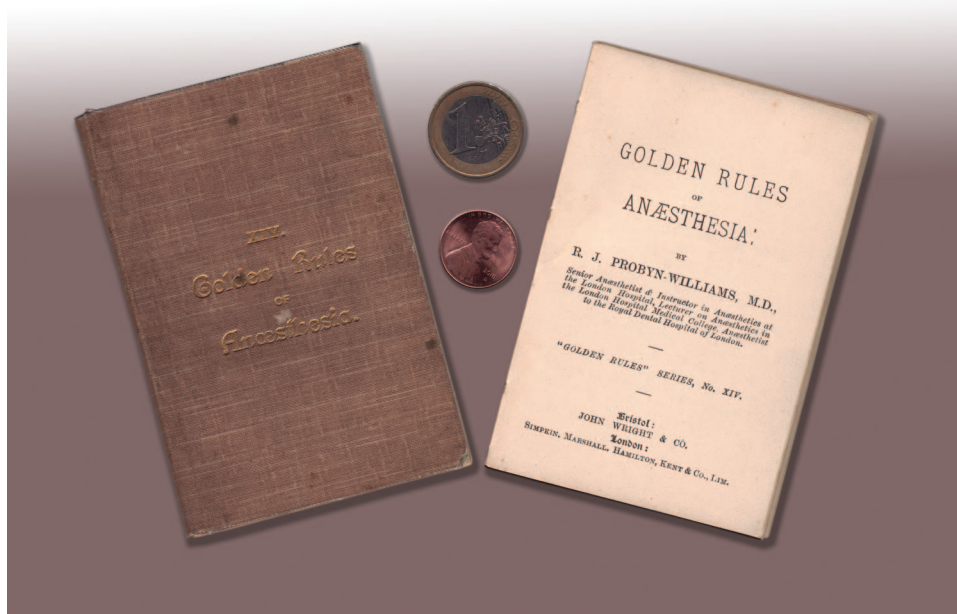
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ANESTHESIOLOGY REFLECTIONS

Tiny But *Golden Rules of Anaesthesia*



Published in 1904 from Bristol and London, this first of three editions of No. XIV in the “Golden Rule” clinical series was sized to fit the “waistcoat pocket” of medical students or “occasional anaesthetists.” At 104 × 70 × 7.4 mm, *Golden Rules of Anaesthesia* followed 67 numbered pages with 5 advertising ones, all sized 1/32 (“thirty-twomo” or “trigesimo-secundo”) of a printer’s uncut free sheet. Compare the book’s size (above) with that of a U.S. penny or a 1 Euro coin. Two-time P. M. Wood Fellow Rajesh Haridas considers *Golden Rules* “the smallest English-language book on anaesthesia.” The tiny book’s author, Robert James Probyn-Williams (1866–1952), advised readers to “Never give an anaesthetic without a third person being present [or] being prepared with another [anaesthetic, or] having at hand [emergency] apparatus.” Curiously, he also noted that “when your patient is cyanosed, dark blood will make the surgeon’s work more difficult.” (Copyright © the American Society of Anesthesiologists, Inc. This image also appears in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

George S. Bause, M.D., M.P.H., Honorary Curator, ASA’s Wood Library-Museum of Anesthesiology, Park Ridge, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.