Abnormal placentation

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ABSTRACT

The term “morbidly adherent placenta” has recently been introduced to describe the spectrum of disorders including placenta accreta, increta and percreta. Due to excessive invasion of the placenta into the uterus there is associated significant maternal morbidity and mortality. Most significant risk factors for morbidly adherent placenta include history of prior cesarean delivery as well as placenta previa in the current pregnancy. Ultrasound remains the gold standard for antenatal diagnosis, however, in recent years MRI has assisted in identifying complex parametrial involvement. Optimizing maternal and neonatal outcomes involves early prenatal diagnosis, a multi-disciplinary team-based approach, and referral to an experienced center.

Introduction

Definitions

Abnormal placental invasion into the uterine wall is one of the many causes of major obstetrical hemorrhage. In normal placentation, the placental-endometrial interface is separated by a fibrinoid layer (Nitabuch’s layer), preventing excessively deep implantation into the uterine wall. The Nitabuch later provides a cleavage plane, allowing a normal third stage of labor. When this layer of fibrin between the boundary zone of the endometrium and cytotrophoblastic shell of the placenta is disrupted, an abnormally adherent placenta can form.1

The term “morbidly adherent placenta” (MAP), is an umbrella term often used to describe a spectrum of pathologic placental invasion into the uterine wall. The depth of invasion into the uterine wall allows for grading of abnormal placental attachment:

- **Placenta accreta:** placental chorionic villi invade the desidua basalis, and attach to the myometrium
- **Placenta increta:** placental chorionic villi invade into the myometrial wall
- **Placental percreta:** placental chorionic villi fully penetrate the myometrial wall, breaching the serosa and invading into surrounding structures (e.g. bladder, broad ligament, sigmoid colon).

Incidence

The incidence of MAP over the past four decades has increased, quoted to be approximately 1 in 4000 deliveries in the 1970s,2 to 1 in 2500 in the 1980s and 1990s.3 Recent data has demonstrated the endemic has continued to rise, most recently citing the incidence of 1 in 533 deliveries.4 This alarming statistic was most significantly attributed to the increasing prevalence of cesarean deliveries.
Risk factors

The most important step to ensure that patients with suspected MAP are identified prenatally is taking a thorough medical and surgical history. While imaging studies can be helpful adjuncts, all obstetric patients should be screened for clinical risk factors, the presence of which should alert providers to a heightened level of surveillance. In 2004, a twenty-year analysis and matched case-control study out of The University of Chicago sought to determine whether the rate of MAP was rising in conjunction with cesarean section rates. They found the risk of placenta accreta with 2 or more prior cesarean scars increased 8-fold, and the odds for those with a previa increased 51-fold. Additional significant risk factors included advancing maternal age (OR 1.13, 95%, CI 1.089–1.194, p < 0.001).4 This data was supported by a large prospective observational study a few years later in 2006. In those women with a placenta previa, the risk for placenta accreta was 3%, 11%, 40%, 61% and 67% for first, second, third, fourth and fifth repeat cesarean sections respectively. In comparison, in the setting of no placenta previa, the risk for placenta accreta was 0.03%, 0.2% and 0.1% for the first, second and third cesarean section, respectively; and this risk was 0.8% for the fourth and 5th cesarean section. However, after having five or more cesarean sections, even without a placenta previa, the risk for placenta accreta increased to 4.7%.5

The concept of trauma to the endometrium resulting in a future vulnerable placental implantation site has been studied similarly in other gynecologic procedures. In recent years, emerging data has demonstrated that implantation of the gestational sac into a previous cesarean scar could be the precursor to a MAP.6–8 Early studies have demonstrated that prior myomectomy has not been associated with higher risk of placenta accreta.9 However, a recent large population-based study looking at primiparous women demonstrated a strong association between a range of gynecologic procedures and the development of a MAP with increasing risk for abnormal placental invasion as the number of prior gynecologic procedures increased. Prior gynecologic procedures assessed were gynecologic laparoscopy with instrumentation of the uterus; hysteroscopy, including operative hysteroscopy; curettage, including suction curettage and surgical termination; and endometrial ablation. This association was dose dependent, with a fivefold increase in risk for an abnormally adherent placenta for women with a history of three or more gynecologic procedures.10 Other reported risk factors for a MAP include advanced maternal age,9 IVF pregnancy,11,12 as well as hypertensive disorders and smoking.13

The presence of the above risk factors should raise the index of suspicion for MAP. Careful sonographic assessment for markers of abnormal placental adhesion should be performed, and adjunctive imaging with MRI should be considered.

Complications and clinical outcomes

Maternal

Findings from previous studies confirm that a MAP increases the risk of severe adverse outcomes for both mothers and babies (Table 1). A recent population-based study demonstrated an 18-fold greater risk of maternal morbidity, ostensibly associated with delivery, after adjusting for other pregnancy characteristics.14 Maternal death may occur in up to 7% of women with placenta percreta.15

Overall, multiple maternal morbidities have been associated with MAP, including a substantial increased risk of hemorrhage (aOR: 16.6, 95% CI: 13.4–20.5), hysterectomy (aOR: 950.6, 95% CI: 632.9–1427.9), transfusion (aOR: 41.8, 95% CI: 33.4–52.2), anemia (aOR 15.1, 95% CI: 10.8–21.0), abdominal organ injury (aOR: 8.2, 95% CI: 5.2–13.1), bladder surgery (aOR: 38.5, 95% CI: 21.8–68.1), mechanical ventilation (aOR: 63.2, 95% CI: 28.4–140.6) and intensive care unit admission (aOR: 41.3, 95% CI: 30.0–56.9).16 Common genitourinary comorbidities include cystotomy (15% of cases) and ureteral injury (2% of cases).17 Up to 26% of cases can result in admission to the intensive care unit.

Substantial intraoperative blood loss is not uncommon for patients with a MAP, with average blood loss estimates ranging from 2000 mL to 5000 mL.18 Rates of blood transfusion have been quoted from 38%19 to 95%.20 With high rates of transfusion, come associated morbidities such as infections, thrombotic events and end organ damage.21

With increasing depth of placental invasion into the myometrium risk for adverse outcomes increases. Placenta percreta is associated with a greater frequency of significant maternal morbidity than placenta accreta- with significant maternal morbidity being 3 times more frequent in patients with percreta than those with accreta/incrèta.22

The risk for mortality and severe maternal morbidity necessitates careful preparation for delivery by an experienced multidisciplinary team. At-risk patients should be counseled about these risks and prepared for a delivery that ensures precautions have been taken to optimize maternal safety.

Neonatal

The presence of a MAP has been demonstrated to be an independent risk factor for perinatal mortality (aOR 8.2; 95% CIs

| Table 1 – Complications of morbidly adherent placenta. |
|---------------------------------|------------------|
| **Maternal**                    | **Neonatal**     |
| Hemorrhage                      | Still birth      |
| Hysterectomy                    | Neonatal death   |
| Transfusion                     | Late preterm birth|
| Anemia                          | Small for gestational age |
| Abdominal organ injury          |                 |
| Genitourinary comorbidities – cystotomy, ureteral injury |        |
| Mechanical ventilation          |                  |
| Intensive care unit admission   |                  |
| Infection                       |                  |
| Venous thromboembolism          |                  |
| End-organ damage                |                  |
| Maternal death                  |                  |
CI 6.4–10.4, p < 0.001). Studies have demonstrated substantial increases in both the risk of stillbirth (RR 5.4, 99% CI 4.0–7.3) and neonatal death (RR 8.0, 99% CI 1.5–41.6). Causes of stillbirth included preterm premature rupture of membranes, congenital abnormalities, antepartum hemorrhage and infection. Notably, over 90% of still births occurred prior to 32 weeks gestation.

Additionally found is that a MAP is an independent risk factor for late preterm birth (aOR 1.4; 95% CI 1.1–1.7, p = 0.002) and small for gestational age babies (27.3% versus 14%, P < 0.001, odds ratio 5.05, 95% confidence interval 1.46–3.28).

**Diagnosis**

**Clinical presentation**

Optimal outcomes for patients with MAP are achieved with antenatal diagnosis, however, recent studies have reported that up to 70% of cases were diagnosed at time of delivery. Abnormal placental invasion should be included on the differential when the placenta fails to detach from the uterine wall following delivery. The classic antepartum presentation is described as painless, bright red vaginal bleeding in the setting of incomplete placental separation.

**Ultrasonography**

Ultrasonography has continued to be recommended as the mainstay modality in antenatal diagnosis of a MAP. Careful attention to patient history can facilitate earlier imaging.

Some cases of placenta accreta may have resulted from a cesarean scar ectopic pregnancy, which can be identified and treated in the first trimester. In a retrospective study of 94,230 patients – 20 of whom were ultimately diagnosed with placenta accreta at the time of delivery – noted 6 of 7 patients with first trimester ultrasound demonstrating a gestational sac located in the lower uterine segment (Fig. 1), as opposed to a fundal location. Classically, ultrasound features of abnormal placental invasion include (1) the presence of irregularly shaped lacunae in the placenta, (2) thinning of the myometrium adjacent to the placenta, (3) loss of the retroplacental sonolucent line (Fig. 2(A)), and (4) turbulent blood flow through the lacunae on Doppler ultrasound. Suspicion for bladder involvement is based on protrusion of the placenta into the bladder and increased vascularity of the uterine serosa–bladder interface. Several studies have reported on efficacy of sonographic markers of placental invasion. Loss of boundary between the bladder and placenta (Fig. 2(B)) has been found to have highest specificities, ranging from 99 to 100% while turbulent blood flow on color Doppler has shown highest sensitivities, ranging from 89 to 100%. In an attempt to standardize diagnosis and communication for the abnormally invasive placenta, published consensus statements and expert opinions have been developed amongst the community.

Many studies have been conducted to assess the utility of ultrasonography for the diagnosis of abnormal placentation with sensitivities reported anywhere from 67 to 97% and specificity ranging from 50 to 98%. Overall, a recent meta-analysis reported sonographic sensitivity to be 86.4% and specificity to be as high as 94.2%. When compared to MRI, ultrasonography is more readily available, less expensive and non-invasive; however, in recent years there has been a trend to utilizing this additional radiographic modality. In two systematic reviews and meta-analysis, the diagnostic value of ultrasound imaging and MRI in detecting placenta accreta was found to be comparable.

**MRI**

The use of MRI in antenatal diagnosis of placenta accreta has continued to rise. Common MRI findings include (1) abnormal uterine bulging (Fig. 3(A)), (2) heterogeneous signal intensity within the placenta, (3) dark intraplacental bands on T2-weighted images (Fig. 3(B)), (4) focal interruption of the myometrium and (5) tenting of the bladder. Overall, the reported sensitivity of MRI is 78–88%, with a specificity of

**Fig. 1** – Cesarean section scar ectopic pregnancy. Initial scan at 9 weeks demonstrated pregnancy located in the lower uterine segment, with an empty myometrium above.

**Fig. 2** – Morbidly adherent placenta on ultrasonography. (A) Absence of retroplacental clear space at the level of the cesarean scar where the placenta is invading the myometrium. (B) Obliteration of the bladder-uterine interface with loss of the hypoechoic retroplacental zone.
MRI appears to be particularly valuable for defining the boundaries of adjacent anatomic structures and assessing the degree of placental invasion, for example in cases of parametrial involvement (Fig. 3(C)) and cervicotrigenal vascular hyperplasia, allowing for changes in the surgical tactical approach.

Serologic markers

Variation in concentrations of certain serum biomarkers have been found in women with morbidly adherent placentas. In an early retrospective review, women with placenta accreta, increta, and percreta were found to have elevated levels of maternal serum alpha-fetoprotein (MSAFP), a finding that was confirmed in follow-up studies. Abnormally elevated levels of free beta-hCG have also been observed. Recent pilot studies have suggested that the amount of cell-free fetal DNA in the maternal serum could be predictive for invasive placentation, however, this diagnostic benefit has yet to be confirmed. At present, serologic markers are not considered a necessary component in the work-up in women with a suspected morbidly adherent placenta.

Antepartum surveillance

Recommendations for antepartum surveillance will vary according to the clinician’s assessment of risk. Concerns for adverse outcomes are greatest in the presence of maternal placental bleeding. For this reason, providers commonly recommend bed rest and/or restricted physical activity and avoidance of intercourse, particularly in the setting of placenta previa. For patients presenting with new vaginal bleeding and/or threatened preterm labor, inpatient admission and hospitalization is recommended. This allows for closer surveillance and rapid intervention in the event of possible maternal deterioration as well coordination of care with a multidisciplinary team.

There is limited data on clinical outcomes to guide recommendations for antenatal testing. In many cases, testing recommendations might be based on concomitant diagnoses such as placenta previa. In others, serial assessment of fetal growth and weekly antenatal testing is reasonable based on concerns for adverse perinatal outcomes.

Timing of delivery

Delivery timing depends on the antenatal clinical course, and requires a thoughtful balance of optimizing both maternal and neonatal outcomes. In those patients delivered in the preterm period, antenatal corticosteroids should be administered to enhance fetal lung maturity. In the setting of a placenta previa and possible morbidly adherent placenta, delayed delivery could possibly increase the risk of maternal bleeding and/or preterm labor. A recent retrospective review demonstrated that women undergoing urgent delivery have worse outcomes. Timing strategies for delivery of a MAP have been analyzed at various gestations from 34 to 39 weeks.
A decision analysis suggested that delivery at 34 weeks is the preferred strategy to reduce adverse maternal outcomes. Although recent studies have demonstrated that those patients with no concern for percreta or increta or no prior cesarean section may also be candidates for later delivery in the late preterm period. Women with multiple episodes of antepartum bleeding or bleeding prior to 32 weeks gestation are at increased risk for emergent delivery. In these patients, delivery timing should be determined on a case by case basis in order to optimize maternal and fetal outcomes.

Multi-disciplinary involvement/planning

Patients with MAP present with a myriad of maternal risks—most significantly hemorrhage, surgical damage and end-organ damage. Because of this, the American College of Obstetricians and Gynecologists recommends collaborative multi-disciplinary delivery planning involving obstetricians, anesthesiologists, pelvic surgeons, vascular surgeons, interventional radiologists and neonatologists. Multiple recent studies have demonstrated improved maternal outcomes with implementation of a multi-disciplinary, team based approach. Additionally, the Society of Maternal Fetal Medicine have created preoperative checklists, as a helpful tool for providers involved.

Anesthetic considerations/management

Both duration of the surgical case and estimated blood loss are important considerations when deciding on type of anesthesia. The American Society of Anesthesiologists Task Force on Obstetric Anesthesia recommends neuraxial anesthesia as the preferred initial approach. Most patients are able to tolerate both prolonged surgery and significant blood loss under epidural anesthesia, with conversion to general anesthesia when clinically indicated. Conversions rates to general anesthesia have been reported anywhere from 29% to 44%. In the context of significant bleeding necessitating massive fluid resuscitation, endotracheal intubation and mechanical ventilation may be considered. For a more detailed discussion of anesthesia considerations, please refer to the chapter Postpartum hemorrhage: Anesthesia Management.

The average blood loss for cases complicated by MAP ranges from 2000 to 5000 mL, and in some studies over 40% are over 5000 mL. This catastrophic hemorrhage requires massive blood product transfusions of various products. In one recent retrospective study assessing transfusion requirements of patients with MAP 95% of women received a red blood cell transfusion and of these more than one third required more than 10 units. To better understand the transfusion needs of patients with MAP, and to evaluate the extent of blood product utilization a recent large retrospective review was performed at a high volume referral center. They found that the percentage of patients receiving blood products were 71% (placenta accreta), 82% (placenta increate) and 82% (placenta percreta). Intraoperative cell salvage has also recently been introduced for patients at high risk for obstetric hemorrhage and placenta accreta. This has been shown to result in lower intraoperative volume of crystalloid and colloid infusion, as well as a shorter length of postoperative hospital stay in patients with placenta accreta. It is already established that identifying patients at highest risk for postpartum hemorrhage, particularly in the setting of MAP, is an imperfect science. However, some centers have utilized standardized preoperative checklists, including prompts for transfusion medicine support, to optimize best practices and improve patient outcomes. Additionally, prompt notification and communication with the blood bank and transfusion medicine teams is essential in ensuring early and aggressive resuscitation. Please refer to the chapter Postpartum hemorrhage: Blood product management, Massive Transfusion.

Pelvic surgeons considerations/management

Due to complex dissection and possible dense adhesive disease, the surgical team should involve providers with an expertise and skill set in this area. Whenever possible, gynecological oncologists and/or urogynecologists should be involved in emergency and complex cases. Pelvic surgeons play an essential role in managing postpartum hemorrhage, particularly with emergency peripartum hysterectomy. Recent studies have shown that up to 75% of emergent peripartum hysterectomies are performed with involvement of a gynecologic oncologist.
Urologic considerations/management

Among hysterectomies performed for MAP, rates of urinary tract injury may be as high as 30%. Particularly for cases in which bladder involvement is suspected, immediate preoperative cystoscopy may be indicated to confirm bladder invasion. Recent studies demonstrate that ultrasound and cystoscopy appear to have similar test validity for prenatal diagnosis for abnormally invasive placentas. Additionally, placement of ureteral stents immediately prior to surgical dissection may assist in preventing urinary tract injury during complex pelvic dissection. Last, placement of a 3-way foley catheter can allow for back filling of the bladder, allowing for improved visualization of planes near the vesicouterine peritoneum.

Vascular considerations/management

Historically, data on precesarean prophylactic balloon occlusion catheters included case reports and retrospective studies that demonstrated uncertain or no benefit. These findings were recently confirmed in a large randomized controlled trial. When utilized, uterine arterial blood flow is occluded by placement of occlusion catheters via the femoral artery into the common iliac artery by interventional radiologists. Intraoperatively, the balloon can be inflated, either as a matter of protocol prior to a portion of the surgery during which a large quantity of blood loss is anticipated, or in the setting of acute hemorrhage. Buttock claudication is the most commonly attributed side effect, which can be decreased by shorter occlusion time.

Pelvic devascularization with embolization remains an area of uncertainty. Embolization is effective for decreasing blood flow through vessels in which active extravasation of blood is identified. Embolization has also been utilized to systematically occlude vessels that supply the placenta in cases of planned interval hysterectomy. There is insufficient evidence to establish which patients most benefit from this approach, however it is likely that only patients who would incur a particularly high risk of severe morbidity or mortality from immediate dissection of an invasive placenta should be considered candidates.

Hysterectomy

Surgical considerations

Various surgical techniques have been suggested to optimize anatomical exposure and dissection. Traditionally a Pfannenstiel skin incision is used for cesarean delivery. However, to visualize structures deep in the pelvis and to perform complex dissection in the case of percreta, a vertical skin incision is necessary to ensure adequate exposure. When placenta accreta is suspected, performing delivery through a vertical incision is recommended. Performing a vertical incision once a Pfannenstiel incision has been made (i.e., a “T” skin incision) often results in poor wound healing due to devascularization of the skin towards the midline. Avoiding hysterotomy placement close to the placental attachment can significantly reduce blood loss. Intraoperative ultrasound assessment using a sterile probe cover can aid in placental localization and help map the optimal location for hysterotomy incision. A fundal or posterior incision may be necessary. The uterus can be delivered through the skin incision and exteriorized to facilitate safely performing the hysterotomy and delivery of the fetus.

Risks of attempted placental removal

The desire to preserve future fertility and possibly avoid hysterectomy poses a challenge for obstetricians at the time of delivery. Diagnosis of abnormal invasive placenta is made based on histopathological criteria specifically complete or partial absence of the decidua with villi directly embedded in the myometrium. Confirmation of diagnosis is possible microscopically, following cesarean hysterectomy. Attempts at manual removal of the placenta can distort the spatial relationship between the accreta villous tissue and the uterine wall, making confirmation of diagnosis difficult. Additionally, avoiding attempted placental removal has been associated with reduced maternal morbidity in women with suspected placenta accreta. Recent studies have demonstrated that women with placenta accreta, increta or percreta who have no attempt to remove their placenta, have reduced rates of hemorrhage (median estimated blood loss 2750 versus 6100 ml, p = 0.008) and reduced need for blood transfusion (59 versus 94%, p = 0.014). Therefore attempted removal of the placenta is not recommended.

Evidence for interval hysterectomy

Recent practices have introduced the option of delayed or “interval” hysterectomy to delivery planning. In this management approach, the placenta is left in situ following delivery of the neonate, with plan to proceed with hysterectomy weeks later. In some cases, selective embolization of placental vessels may be performed by experts in vascular interventions. Providers have opted for this approach in hopes that time will allow for regression of the placental bulk, and the risk of hemorrhage will be reduced at the time of hysterectomy. This approach may be particularly favorable in cases of extensive placental invasion involving adjacent structures, such as parametrium, when dissection would result in hemorrhage, require a great deal of time, and post a high risk for vascular or organ injury. A recent retrospective review proposed improved outcomes for patients with placenta percreta who underwent delayed hysterectomy when compared to immediate hysterectomy. The benefit of potential regression must be weighed against the risk of hemorrhage, infection, and, when used, the procedure-related complications of vascular embolization procedures (for example, unintended embolization of adjacent structures with possible vascular compromise).

In some instances, such as hemorrhage or severe infection, it may be necessary to perform a hysterectomy under urgent or emergent circumstances. Given the substantial risks for severe morbidity and mortality in these cases, delayed hysterectomy should be reserved for women who are highly motivated, properly counseled and able to adhere to close follow-up with highly experienced and equipped centers.
Evidence for conservative management

Some centers have advocated for “conservative” management of MAP to reduce surgical complications and preserve fertility. Conservative management is defined as leaving the adherent placenta in situ after delivery of the neonate and awaiting involution and separation of the placenta. In attempting conservative management, selective arterial embolization has been utilized in an attempt to decrease uterine blood flow to the retained placenta and to precipitate placenta involution. Additionally adjuvant methotrexate, a dihydrofolate reductase inhibitor targeting rapidly dividing cells, has been used assist with placental expulsion. However, placental cell division in the third trimester is limited and outcomes do not appear different. Whether it be using embolization or methotrexate for adjuvant therapy, a recent review of the literature has demonstrated uncertain benefit, which was supported in an expert panel review.

Common complications of conservative management include infection, delayed postpartum hemorrhage, disseminated coagulation, and unplanned emergency reoperation.

Management of unanticipated MAP

The management of an unanticipated MAP poses a significant challenge for clinical teams. If there is concern for abnormal placentation prior to hysterotomy and delivery is non-emergent it is important for the multidisciplinary team to pause and assess options. These options may include covering the uterus with warm laparotomy sponges and awaiting assistance or additional equipment to arrive in the operating room, or closing fascia and skin and transferring the patient to a tertiary hospital with experience managing these complicated surgeries.

If after consideration or there is an urgent need to proceed it is important to assess for alternate hysterotomy sites, including fundal and or posterior incisions, to avoid disrupting the placenta.

Early recognition and involvement of a multidisciplinary team is essential in optimizing maternal outcomes. The first step is to notify members of the care team about the potential diagnosis in order to facilitate mobilization of resources. The patient and/or immediate family member should be informed of the diagnosis and made aware of the gravity of the situation. The potential for hysterectomy should be discussed and informed consent obtained as appropriate for the acuity of the situation. Immediate steps taken by the care team should include the following:

- Notification of the blood bank team, and possible activation of a massive transfusion protocol, to ensure early and aggressive resuscitation with blood products.
- If not already administered, tranexamic acid should be given.
- Additional anesthesia support to manage hemodynamics including insertion of additional peripheral, central, and arterial lines and administration of blood products and/or vasoactive medications. Conversion of regional to general anesthesia is likely in high-risk circumstances.
- Early consultation of surgical subspecialists, including gynecological oncologist and possibly urologists and vascular surgeons. Additionally, obtaining a second and/or more experienced surgical technician can be helpful.
- Early opening of additional surgical instruments for exploratory laparotomy and possible hysterectomy. Also, obtaining hemostatic agents including Floseal, Gelfoam, Surgifoam, Surgicel and Thrombin.

Conclusions

In conclusion, the morbidly adherent placenta is one of the most catastrophic causes of antenatal and postpartum hemorrhage in obstetrics. With the rising incidence of cesarean deliveries and gynecologic procedures, a parallel rise in the frequency of MAP may be anticipated. Decreasing maternal morbidity and mortality requires heightened suspicion and surveillance for MAP as well as a collaborative and multidisciplinary approach to detailed preoperative planning. Referral to a tertiary care center with access to specialists in maternal-fetal medicine, surgical subspecialties, anesthesia, transfusion medicine, and intensive care is recommended to ensure optimal outcomes for these complicated patients.

REFERENCES


