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Title/Running title: Failed manual removal of the placenta after vaginal delivery

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ABSTRACT

Purpose: A retained placenta after vaginal delivery where manual removal of placenta fails is a clinical challenge. We present six cases that illustrate the heterogeneity of the condition and discuss the etiology and terminology as well as the clinical management.

Methods: Members of the European Working group on Abnormally Invasive Placenta (EW-AIP) were invited to report all recent cases of retained placenta that were not antenatally suspected to be abnormally adherent or invasive but could not be removed manually despite several attempts.

Results: The six cases from Denmark, the Netherlands and the UK provide examples of various treatment strategies such as ultrasound-guided vaginal removal, removal of the placenta through a hysterotomy and just leaving the placenta in situ. The placentas were all retained but it was only possible to diagnose abnormal invasion in the one case, which had a histopathological diagnosis of increta. Based on these cases we present a flow chart to aid clinical management for future cases.

Conclusion: We need properly defined stringent terminology for the different types of retained placenta, as well as improved tools to predict and diagnose both abnormally invasive and abnormally adherent placenta. Clinicians need to be aware of the options available to them when confronted by the rare case of a retained placenta that cannot be removed manually in a hemodynamically stable patient.

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KEYWORDS

- Retained placenta
- Manuel removal of placenta
- Abnormally invasive placenta
- Placenta accreta

INTRODUCTION

Retained placenta (RP) after vaginal delivery is a complication known to cause maternal morbidity and mortality. The immediate hazard of RP and subsequent attempts at manual removal is severe postpartum hemorrhage (PPH). Emergency hysterectomy, circulatory collapse and maternal death may be a consequence. Long-term complications of PPH are, among others, anemia, failure to lactate and postpartum depression (1). The pathophysiology of the condition is heterogeneous. RP may be categorized as 1) a normal placenta entrapped due to a contracted cervix or a structural uterine abnormality, 2) a normal placenta still adherent due to failed contraction of the retroplacental myometrium, or 3) an abnormally adherent (accreta) or invasive (increta or percreta) placenta also known as 'placenta accreta spectrum' (PAS) (2). Consensus regarding the treatment of RP has been hard to achieve, perhaps due to difficulty in discriminating between the aforementioned causes. However regardless of the cause, manual removal of placenta (MROP) under regional or general anesthesia is recommended when active management, i.e. uterotonics and controlled umbilical cord traction fails, the placenta remains in situ and there is no strong antenatal suspicion of abnormally adherent or invasive placenta.

When the retained placenta is abnormally adherent (accreta) or abnormally invasive (increta/percreta), manual removal is extremely difficult or even impossible. In cases of retained placenta due to failed contraction or entrapment, manual removal is usually a simple and blind procedure.

The present article presents six patients with RP after vaginal delivery where manual removal was not possible despite several attempts by experienced obstetricians. There had been no antenatal suspicion of PAS in any of the cases, therefore attempting MROP was appropriate clinical practice as was abandoning the attempts when it became apparent that the placenta could not be removed safely. The women were hemodynamically stable, without excessive bleeding. The supervising clinicians therefore opted for uterus-preserving management.

This article has two aims: Firstly, we present and discuss the considerations for maneuvers and interventions following failed MROP in the hemodynamically stable patient. These situations are rare and heterogeneous, therefore it is highly unlikely that evidence based recommendations will become

available, making case reports important. Secondly these cases help demonstrate the inadequacy of our current definition of, and classifications for, the types of retained placenta. The gold standard for diagnosis of PAS is histopathological examination, according to the presence and degree of trophoblastic invasion. This is however, not possible if the placenta is left in situ. In these cases diagnosis must solely rely on imaging findings (sonographic or magnetic resonance imaging (MRI)) and clinical presentation. Only one of our six cases had tissue available for histopathological examination, this demonstrated evidence of abnormal placentation. None of the cases presented had typical imaging signs for PAS when examined both antenatally and postnatally using ultrasound/MRI. A suggestion for a clinical grading system to assess severity of the abnormally adherent and invasive placenta was recently published (3). Using this system, the cases presented would be classified as either grade 2 which is defined as "MROP required and parts of placenta thought to be abnormally adherent" or grade 3 defined as "MROP required and the whole placental bed thought to be abnormally adherent" (3).

MATERIALS AND METHODS

Members of the EW-AIP were invited to report all their recent cases of vaginal delivery with a retained placenta following failed attempts at MROP where the women were hemodynamically stable thereby allowing consideration of how to proceed without emergency hysterectomy. We collected a total of six cases from Denmark, the Netherlands and the UK.

RESULTS

Case 1: Successful removal of placenta from a septate uterus under ultrasound guidance

A 33-year-old Gravida 2, Para 0, with a history of missed miscarriage treated by dilatation and curettage (D&C). Previous hysterosalpingography had shown a possible occlusion of the right salpinx, and the patient recalled being told that she had a "heart-shaped" uterus. In the index pregnancy, the patient contacted the delivery ward twice close to term with a constantly burning pain on the right side of the uterine fundus. An ultrasound scan of this area showed no abnormalities. After she delivered, the placenta remained in situ. Manual and instrumental removal of placenta was attempted unsuccessfully twice within 24 hours and an intrauterine balloon device was inserted to minimize blood loss. Her vaginal bleeding was not excessive. On an ultrasound scan, a bicornuate uterus with a septum was seen and the placenta appeared to be in the right corner. There were no sonographic signs of abnormally invasive placentation. A third attempt was made to remove the placenta vaginally on the forth day post partum. Under ultrasound guidance, the placenta was removed manually and by inserting tissue forceps into the plane of cleavage, carefully separating the remaining placental tissue from the uterine wall in multiple small fragments. Histologic examination of the placental tissue removed showed no abnormalities. The patient was discharged four days after the procedure with no signs of infection and minimal vaginal bleeding. A follow-up ultrasound scan three months later showed an empty partial septate uterus (ESHRE Class U2). The upper right corner of the now empty uterine cavity had a blurred lining between the endometrium and the myometrium, this was suspected to have been the site of the placental implantation.

Case 2: Retained placenta delivered vaginally in many small fragments under ultrasound guidance

A 30-year-old Gravida 2, Para 1, had one previous vaginal term delivery complicated by MROP with a PPH of approximately 3000 ml. After the second delivery the placenta was again retained. Two experienced physicians attempted MROP unsuccessfully 55 minutes after delivery of the neonate. An intrauterine balloon tamponade was inserted, and the patient was stabilized. The blood loss at this point was 3200 ml. The balloon was removed the following day, and bleeding was not excessive. An ultrasound scan showed a retained placenta with no signs of abnormally invasive placentation. The patient received four blood transfusions and broad-spectrum antibiotics. Five days later another attempt to remove the placenta was made after informing the patient of the risk of emergency hysterectomy in case of severe bleeding. Tissue forceps and curettage were used under ultrasound guidance and the placental tissue was successfully removed in multiple small fragments. The patient was discharged the next day but returned the same evening with fever. She received another 24 hours of intravenous antibiotics, followed by seven days of oral antibiotics for suspected endometritis. There were no further adverse events. When followed up three months postpartum, the patient had no gynecological complaints; she was breastfeeding and had regular menstrual periods using combined oral contraceptive pill. On an ultrasound scan an area of retained placental tissue was seen in the uterine fundus, therefore the patient was booked for a hysteroscopy. Placental tissue was resected from the posterior wall of the cavity. Histopathological examination of the placental tissue removed by ultrasound-guided forceps and curettage, and subsequently by hysteroscopy, was not reported as demonstrating evidence of PAS.

Case 3: Retained placenta left in situ after several attempts of manual removal. Placenta fully absorbed nine months postpartum without adverse events

A 36-year-old Gravida 8, Para 1, with a history of previous surgery to remove a septum from a bicornuate uterus, six miscarriages all treated by D&C and a vaginal delivery preterm at 27 weeks of gestation. In the index pregnancy she was scanned antenatally by a fetal medicine doctor with considerable expertise in diagnosis of PAS, they felt that there were no ultrasound signs suggestive of abnormal placentation. Labor was induced due to preterm premature rupture of membranes (PPROM) at 31 weeks of gestation. After vaginal delivery the placenta did not separate spontaneously. Two experienced obstetricians attempted MROP unsuccessfully. The patient was given synthetic oxytocin and an intrauterine balloon device was inserted. Total blood loss was 900 ml. Bleeding was not excessive after removal of the balloon the following day. The placenta was left in situ and the patient was discharged having been given prophylactic oral antibiotics for seven days. The patient was scanned monthly until the placenta was completely reabsorbed. Once the placenta appeared fully absorbed on ultrasound, a serum human chorionic gonadotropin was measured which was was negative. This process took nine months and 11 days. Her blood loss during the follow-up period was minimal and there were no adverse events.

Case 4: Placenta left in situ after attempted manual removal. Patient readmitted nine weeks postpartum with sepsis unresponsive to antibiotics. The placenta was successfully removed with tissue forceps under ultrasound guidance.

A 28-year-old Gravida 2, Para 0, with a history of previous first trimester termination of pregnancy by D&C. After a spontaneous vaginal delivery at term, the placenta did not detach and two experienced obstetricians attempted MROP unsuccessfully. During the procedure, the patient bled approximately 400 ml. The patient received prophylactic intravenous antibiotics during the procedure and for the first 24 hours. An ultrasound was performed three days postpartum, which showed no signs of abnormally invasive placentation. The patient was discharged without antibiotics with the intention of monthly follow-up until the placenta was fully absorbed. However, nine weeks later, she was admitted with signs of sepsis (mildly raised white blood cell count, intermittently increased (spiking) temperatures and intermittent tachycardia to 110 bpm). She had no vaginal bleeding or lower abdominal pain. An ultrasound scan showed that the placental bed was now poorly perfused. She remained stable and as after three days of broad-spectrum intravenous antibiotics the symptoms had not resolved, MROP was attempted again. The placental tissue was successfully removed under ultrasound guidance with sponge forceps and gentle manual exploration of the cavity. Ultrasound examination at the end of the procedure demonstrated a clear endometrial echo with no evidence of any retained tissue. The patient made a good recovery and was discharged three days later with no vaginal bleeding. A subsequent serum human chorionic gonadotropin level was negative. Histology demonstrated necrotic tissue of placental origin with no other findings of note.

Case 5: Retained placenta in a bicornuate uterus removed by hysterotomy

A 33-year-old, Gravida 3, Para 1 with a history of a missed miscarriage treated by an uncomplicated D&C and an uncomplicated vaginal delivery at 36 weeks of gestation with 300 ml of blood loss. After another vaginal delivery at 37 weeks of gestation the umbilical cord ruptured during controlled cord traction. Forty minutes later, the patient was transferred to the operating theatre. Two experienced consultants unsuccessfully attempted MROP. Blood loss had by then accumulated to 2000 ml. An intrauterine balloon device was inserted and sulprostone, a prostaglandin analogue, was administered, which stopped the bleeding. As the patient was hemodynamically stable she was transferred to a tertiary care hospital where an MRI scan was performed of the lower abdomen shortly after arrival. This showed the placenta located in the fundal part of the uterus with no signs of abnormally invasive placentation. More than ten hours after delivery, another attempt of MROP was performed. Bleeding was minimal after deflating the balloon tamponade, but the placenta could not be reached vaginally as the cervical dilatation was only three centimeters. A laparotomy was performed through a Pfannenstiel incision. The uterus had a bicornuate shape (ESHRE Class U2) with an enlarged left side where the placenta was located. A median incision was made in the uterus and the placenta was removed in multiple fragments from the left uterine horn. The uterine wall was sutured in layers. The estimated blood loss from the procedure was 4000 ml. The placental weight was 323 grams. No signs of abnormally invasive placentation were found when the placental tissue was sent for histological examination.

Case 6: Sepsis after multiple attempts at manual removal, retained placental tissue finally removed by laparotomy demonstrating adherence to a leiomyoma.

A 34-year-old Gravida 2, Para 1, had one previous uncomplicated vaginal delivery at term. At 33 weeks of gestation into the index pregnancy she experienced PPROM followed by a spontaneous vaginal delivery 3 three days later. The placenta was retained. Two experienced obstetricians performed an unsuccessful attempt of MROP. The following day an ultrasound showed the entire placenta in the right upper corner of the uterine fundus. Abnormally invasive placentation was suspected due to a thin uterine wall. Therefore, the patient was transferred to another tertiary care center with greater expertise in managing PAS. Manual and instrumental removal of the placenta was attempted twice unsuccessfully. An ultrasound scan as well as a MRI scan confirmed large amounts of retained placental tissue in the right corner of the uterine fundus. As she was stable and not bleeding excessively the decision was made to manage her conservatively and leave the placenta in situ. The patient was then referred back to her original delivery unit where she received prophylactic broad-spectrum antibiotics and several blood transfusions. She was discharged home but returned 26 days postpartum with a fever and vaginal discharge. She had no vaginal bleeding or lower abdominal pain. Intravenous broad-spectrum antibiotics were administered and a CT scan confirmed retained placental tissue. A hysteroscopy was performed. The right tubal ostium was completely blocked by necrotic placental tissue. Resection of the tissue was not possible; therefore the surgery was converted to a laparotomy. The right uterine corner, which was grossly enlarged to approximately 8-10 cm in diameter, and a normal right salpinx were removed. The remaining uterus was sutured in layers. Postoperatively the patient received antibiotics and blood transfusions and was discharged few days after surgery. Histological examination of the resected myometrium with attached placenta concluded that the placenta had been located in the upper right side of the uterine cavity, infiltrating the myometrium, this was therefore classified as placenta increta. Furthermore, near the right ostium there was a 5 cm large intramural leiomyoma to which the placenta was accrete adherent. The right salpinx, fimbria and uterine corner were normal.

DISCUSSION

When a placenta is retained after vaginal delivery, there may be several underlying pathophysiological causes. It might be entrapped due to a closing cervix or uterine anomaly, it might not have separated due to failed retroplacental myometrial contraction or it might be abnormally adherent or invasive. This case series presents patients with the following common characteristics; 1) no antenatal suspicion of an abnormally adherent or invasive placenta, 2) a retained placenta after vaginal delivery, 3) failed attempt(s) at MROP by experienced obstetricians and 4) a hemodynamically stable patient, allowing various uterus-preserving management strategies to be considered. These cases are rare and management differed based on expertise, attitude and available resources. None of the cases have been previously published, and to the authors' knowledge, only three similar case-reports have been published (4-6). Based on our cases we designed a flow chart to aid consideration of management after failed manual removal of the placenta (Figure 1).

Management of the cases

When MROP following a vaginal delivery fails in a hemodynamically stable patient without ongoing heavy bleeding, an intrauterine balloon tamponade may be considered in order to buy time to either decide on a management strategy or transfer the patient to a tertiary care facility. However, lack of data on the safety of this procedure implies caution. Advantages of referral to a tertiary facility include having access to advanced treatment modalities, such as pelvic arterial embolization and availability of specialists experienced in complex pelvic surgery (usually gynecological oncologists). Seeking advice from an expert in diagnostic imaging of PAS is also crucial for deciding further management including assessing the appropriateness of further attempts to remove the placenta. Irrespective of the chosen modality, imaging can determine whether the placenta is showing signs of abnormal invasion and can map out the cavity of an anomalous uterus. If subsequent imaging shows signs of PAS, a decision on management should be made after consideration of the expertise and resources available, with full consultation with the woman herself to assess her desire for future fertility. Options include; laparotomy with placental removal through a hysterotomy +/- local resection of the endometrium, a hysterectomy with the placenta left in

situ, or conservative management with the placenta left to reabsorb. If imaging shows no signs of PAS, further ultrasound guided vaginal attempts at removal of the placenta should be considered.

If the placenta is removed through a hysterotomy, the patient will have an increased risk of abnormally invasive placentation in future pregnancies (7). If MROP fails, bleeding is minimal and there are no signs of infection conservative management by leaving the placenta in situ to be reabsorbed may be an option. This strategy was used in three cases; in one the strategy proved successful but it took nine months before the placenta had resolved, in the other two cases the patients developed sepsis and one had a laparotomy. Thus, only one in three patients had a successful conservative management, and even though the uterus was preserved in these three cases we do not have data on the functionality of the uterus. Factors to be taken into consideration before leaving the placenta in situ are the risk of serious life-threatening complications, potential compliance if complications such as hemorrhage or infection arise, logistics such as distance from the patient's home to a hospital and the patient's demand or desire.

Complications

The two main complications in these cases were hemorrhage and infection. Blood loss is an important parameter when comparing treatment strategies however too few cases are presented here to be able to draw definitive conclusions regarding which management strategy best minimizes blood loss. The patient with the greatest blood loss was case number five; treated by removing the placenta from a bicornuate uterus through a hysterotomy the same day as the delivery. She bled approximately 2000 ml while attempting MROP and an additional 4000 ml during the laparotomy. The patient with the smallest blood loss was case number four; initially treated conservatively, however readmitted nine weeks postpartum due to sepsis requiring the placenta to be removed vaginally. She bled minimally prior to discharge, and approximately 400 ml during the vaginal removal.

Four of the six cases developed fever and intrauterine infection at some point in the course of their treatment despite prophylactic antibiotics. This is a greater proportion than has been reported for planned conservative management due to antenatally diagnosed abnormally invasive placentation (8). Although these infections may be attributable to multiple attempts at removing the placenta vaginally, there is no clear consensus as to whether attempted MROP increases the risk of endometritis, and no

studies have been conducted to determine the efficacy of routinely administered prophylactic antibiotics (9).

Risk factors for a retained placenta

In these six cases, the complication of an abnormally adherent placenta was not anticipated including the one patient who had been screened for PAS. On further examination of the patient histories all the women had at least one risk factor for RP. One patient had previously had a retained placenta, which increases the risk of recurrence (10, 11). Three out of the six cases were preterm deliveries, a factor strongly associated with retained placenta (10-14). Previous uterine surgery is a known risk factor and although none had had a previous caesarean section or myomectomy, one had had a resection of a septum in a bicornuate uterus (15, 16). Uterine curettage, previous surgical termination and miscarriages have been identified as a risk factor for RP (10-12, 15, 17). Four of the six patients had a history of at least one D&C. Parity may be a risk factor but several studies report conflicting results (10-15). Four of the women had had one previous baby and two were nulliparous. Congenital uterine anomalies (CUAs) were present in at least three of the presented cases. The prevalence of CUAs in an unselected population is 5.5 %, and higher in a population with infertility and previous miscarriage (18). CUAs have been known to be associated with adverse outcomes in pregnancy, such as recurrent pregnancy loss, low birth weight, preterm birth, hypertensive disorders of pregnancy, malpresentation and caesarean delivery (19-22). To our knowledge, only one study has found an association between CUAs and RP, a finding our cases may support (21).

Use of intrauterine balloon, pelvic arterial embolization and methotrexate

An intrauterine balloon was used in four out of the six cases in an attempt to minimize blood loss. Although a recent review raises concerns about the lack of randomized controlled trials to prove the beneficial effect of intrauterine balloon (23) it has been implemented as an alternative in the surgical treatment for PPH in many obstetric settings due to a number of studies correlating its use to minimizing blood loss and avoiding peripartum hysterectomy (24-28). However current practice is to use an intrauterine balloon in an empty uterus, this is not how it was used in the cases presented in this article. In cases of PAS, where the placenta remains in situ, intrauterine balloon is generally not advised as it may

pose a theoretical risk of tissue disruption and massive bleeding due to compression applied over damaged myometrium (29). This case series cannot comment on the efficacy or the safety of intrauterine balloon in these rare situations, however there were no adverse events.

Pelvic arterial embolization (PAE) is a second-line treatment modality for PPH and is usually available in tertiary referral centers. Although a recent case series and a systematic review concluded that PAE is a highly efficient, safe, fertility preserving treatment, (30) this study does not include a single patient where the cause of PPH is retained placenta. The majority of the patients included, suffered from severe PPH due to uterine atony, the remainder bled secondary to genital hematomas, vaginal tears or arterio-venous malformations. When conducting a search using the MeSH terms “pelvic arterial embolization” and “retained placenta” we found no relevant publications. We do not believe that pelvic arterial embolization would have been an appropriate treatment modality for any of the presented cases, as they did not have ongoing bleeding.

Methotrexate (MTX) is a pharmacological treatment modality that has been applied as an adjunct to attempting conservative management of PAS, while awaiting reabsorption or expulsion (31-35). MTX inhibits the folic acid pathway; thereby targeting rapidly dividing cells, such as trophoblasts. It is therefore more commonly used for ectopic pregnancies and gestational trophoblastic diseases. That MTX can quicken reabsorption or expulsion of a postpartum placenta that is no longer growing seems biologically implausible. The largest cohort of conservatively treated patients with PAS to date conclude that there is no convincing evidence of the efficacy of the drug in these difficult cases (8). MTX is however contraindicated in breastfeeding and more importantly has potentially serious adverse effects, such as pancytopenia or nephrotoxicity. Intraumbilical MTX administration and finally multi-organ failure was the cause of the only maternal death in the aforementioned cohort of 167 patients. We do not believe that MTX should have been used in any of the presented cases.

Limitations

The major limitation of this case series is its size with only six cases reported. Due to the way the cases were collected no comment can be made regarding the incidence of this situation. The EW-AIP however, is made up of over 40 clinicians from 11 European countries all working in tertiary referral units specializing in PAS. The fact that when all of them were asked to report any cases only six were found means it is likely to be a relatively rare situation. Based on the heterogeneity of the cases, it is not possible to comment on the superiority of one treatment over the other, therefore we sought to report the different strategies, which had been employed. As a result of this process we have developed the flow chart (Fig 1) to aid clinicians when faced the same situation. In terms of future fertility, to date there has been no follow-up of the patients and therefore we cannot comment on any subsequent pregnancies.

Challenges in terminology and classifications of the retained placenta

The second aim of this article is to illustrate the inadequacy of the current definitions of and terminology used for the placenta that will not detach in the third stage of labor. The terms 'morbidly adherent placenta' (MAP) (29, 36), 'abnormally invasive placenta' (AIP) (3), 'placenta accreta spectrum' (PAS) (7) or just 'placenta accreta' are used as collective terms for the histopathological diagnoses of placenta accreta, increta and percreta. The degree of abnormal trophoblastic attachment or invasion defines the exact diagnosis; accreta is abnormally adherent, with the villi attaching directly to the myometrium without intermediate decidua, increta and percreta are abnormally invasive, with the villi invading into the myometrium in increta, and through the serosal layer in percreta (7).

These diagnoses should be made prenatally as this has been clearly shown to decrease maternal morbidity and mortality (37). This requires an initial diagnosis based on imaging findings (sonography and/or MRI). The sensitivity and specificity of sonography for detecting PAS are generally good, however the parameters differ depending on the expertise of the operator and the selection of the patient population (7). A vast number of studies on the sonographic appearance of PAS have been published, however there is no consensus on which sonographic signs should be used and how they can be described in an objective, reproducible manner with an acceptable inter-observer variability (38). High sensitivity is crucial as antenatal detection of PAS has a significant impact on the outcome for the patient. However specificity is also important as a false positive diagnosis may come with the price of a vertical laparotomy followed by a hysterectomy costing the patient her fertility (3). MRI is often used to confirm

the sonographic diagnosis and to map the topography of the placental tissue in order to aid in planning the surgical intervention. However, whether MRI can improve diagnostic accuracy or outcome has not been proven to date (29). When PAS is detected prenatally the general recommendation is a planned, preterm caesarean section, leaving the placenta in situ prior to either performing a hysterectomy or attempting conservative management, i.e. closing the hysterotomy after delivering the neonate and then leaving the placenta to reabsorb. Attempts to forcibly remove the placenta are strongly advised against as it may cause massive hemorrhage (36).

If there is no material available for histopathological diagnosis and there has been no imaging performed prenatally specifically to detect PAS, there only remains clinical diagnosis, which is highly subjective and variable. Authors of a recent review of PAS reported that "most authorities only consider cases that require additional surgical interventions to control bleeding, such as hysterectomy, uterine curettage, and embolization of pelvic vessels, to have clinical evidence of accreta" (7) whilst another paper recently published on behalf of NFOSS only considered cases requiring a blood transfusion and laparotomy to be accreta (39). As its name suggests, PAS is a spectrum disorder ranging from abnormal adherence to the full blown invasion of percreta with the least severe, adherent end of the spectrum currently proving to be the hardest to define. In response to this issue an attempt has recently been made to generate a clinically relevant grading system for assessment of severity of PAS (3). Using this scale, all of of the cases would score at least grade 2 (abnormal adherence in parts of the placental bed on attempted MROP) if not grade 3 (abnormal adherence of the entire placental bed on attempted MROP) depending on the exact findings of the obstetrician at the time of MROP. Data is available on this for cases 3 and 4 confirming that they were considered to be grade 3 by the obstetrician attempting the MROP. Although this confirmation is not available for the other four cases it is most likely that they were grade 3 as if they were only partially adherent they would have probably partially separated during the attempt leading to significant bleeding. Therefore, using this scale, all of the cases would be classed as PAS most likely grade 3.

So how should we define our cases? Should they be regarded as part of the PAS as the clinical grading scale suggests? Four of the patients had to have their placentas removed in multiple fragments, which suggests abnormal adherence and one had histopathological findings of placenta accreta and increta therefore this might seem appropriate. In the absence of histopathological results should the clinical

presentation of a placenta that cannot be removed manually suffice to make the diagnosis of PAS? We believe that if the accoucheur is experienced and able to insert their hand into the uterus far enough to grasp the placenta yet still cannot remove it entrapment of a normally separated placenta can be ruled out in a normally formed uterus. Therefore, the most likely reason for an experienced obstetrician abandoning a MROP with the placenta still in situ is failure to find an adequate plane of cleavage to facilitate separating the placenta from the uterus. This is highly unusual and suggests abnormal adherence to the uterine wall fitting with at least a grade three on the suggested clinical grading scale.

One thing is clear if high quality research is to continue into the PAS, diagnosing it in a binary manner (PAS or not PAS) is insufficient. Agreement is urgently needed on a way to distinguish between (a) a normal placenta and (b) an abnormally adherent or (c) invasive placenta that is clinically relevant and can be employed in the absence of histological results. The only such classification that the authors are aware of is the previously published clinical grading scale for PAS (3), which has been adopted by the EW-AIP and is being used to grade severity in the data they collect.

CONCLUSIONS

When a retained placenta cannot be removed manually, the patient is hemodynamically stable and the bleeding controllable; we recommend ultrasonography or MRI to detect abnormally invasive placentation. Provided there are no signs of abnormal placentation an additional manual or instrumental attempt to remove the placenta vaginally can be considered using perioperative ultrasound guidance. If the second attempt fails, the options are to perform a laparotomy with either resection or hysterectomy, or to leave the placenta in situ, taking into account the long term follow up including risk of sepsis or hemorrhage after discharge of the patient. These strategies were associated with successful outcomes in this case series. No international consensus is available for the clinical diagnosis of PAS in the absence of histopathological data, however, using the clinical grading scale employed by the EW-AIP, all the cases presented would be regarded as PAS grade 2 or 3. A flow chart has been devised by the authors to help facilitate management of similar cases in the future.

FIGURE CAPTION

Fig. 1 Flow chart for the management of failed manual removal of a retained placenta. Abbreviations: MROP: Manual removal of placenta, MRI: Magnetic resonance imaging, AIP: Abnormally invasive placentation

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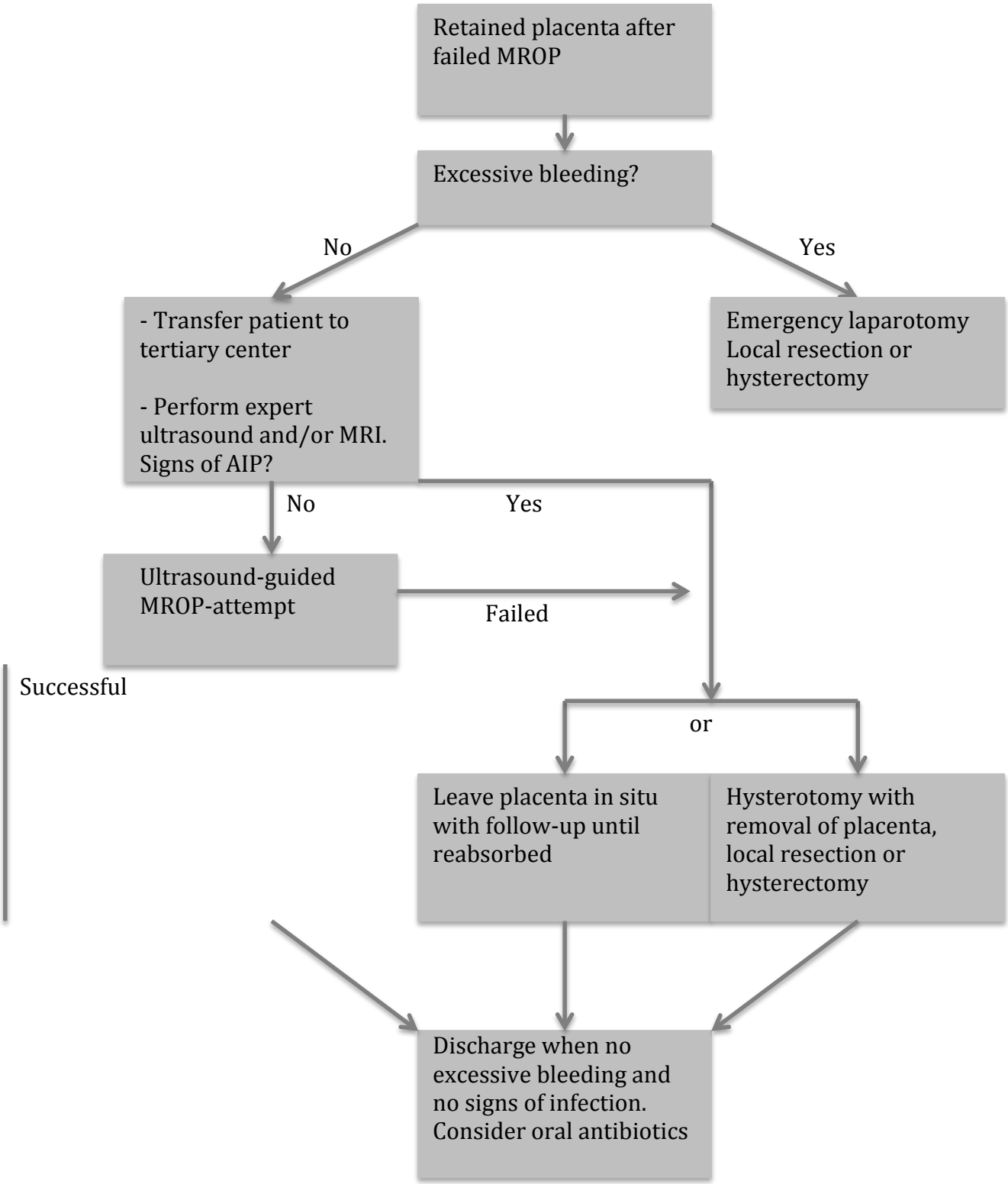

table Click here to download table Table 1 retained placenta 150617.docx

Table 1. Overview of the cases presented. Abbreviations: GA (gestational age) D&C (dilatation and curretage) RP (retained placenta) ESHRE (European Society of Human Reproduction and Embryology) pp (postpartum) MROP (manual removal of placenta) PPROM (preterm premature rupture of the membranes)
* *1 transfusion: 500 ml packed erythrocytes diluted in saline-adenine-glucose-mannitol solution.*

Case no.	Obstetric/Gynecological history	GA (week)	Blood loss (ml) and transfusions	Uterus anomaly	Balloon tamponade	Final treatment of RP
1	Para 0 1 D&C	39	300 at delivery 200 during 1st MROP. 500 during 2nd MROP 400 during succesful vaginal removal of placenta *No transfusions*	ESHRE Class U2	+	Ultrasoundguided MROP 4 days pp
2	Para 1 1 term delivery complicated by retained placenta, MROP and PPH of approx. 3000 ml	39	720 at delivery 2500 during 1st MROP *4 blood transfusions** 900 during succesful vaginal removal of placenta	None noted	+	Ultrasoundguided MROP 5 days pp + hysteroscopy 3 months pp
3	Para 1 6 D&Cs 1 preterm delivery (GA 27 weeks) 1 surgically removed uterine septum	31 (induced due to PPROM)	350 at delivery 550 during attempted MROP *No transfusions*	ESHRE Class U2 (septum surgically removed prior to index pregnancy)	+	Conservative; placenta left in situ for resorption. Fully resorbed after 9 months
4	Para 0 1 D&C	39	Minimal prior to discharge. 400 at vaginal removal of the placenta *No transfusions*	None noted	-	Sepsis during attempted conservative treatment. Vaginal removal of placenta manually and by tissue forceps 9 weeks pp
5	Para 1 1 D&C 1 preterm delivery (GA 36 weeks)	37	2000 prior to and during attempted MROP 4000 during laparotomy *4 blood transfusions**	ESHRE Class U2	+	Removed through uterotomy approx. 10 hours pp
6	Para 1 1 term delivery	33	200 at delivery 200 during 1st MROP 1500 during 2nd MROP 300 during 3rd MROP *2 blood transfusions** 200 during laparotomy *2 more blood transfusions**	Leiomyoma near the right corner of the uterine fundus.	-	Resection of the right uterine corner housing the placenta adhering to a leiomyoma 27 days pp