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The Management of Secondary Postpartum Hemorrhage

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INTRODUCTION

Secondary postpartum hemorrhage (PPH) is defined as excessive vaginal bleeding from 24 h after delivery up to 6 weeks postpartum[1]. Unlike the definition of primary PPH, there is no clear or standard definition for quantity of the blood loss associated with secondary PPH, and clinical expressions of this definition vary from 'increased lochia' to massive bleeding. The diagnosis is therefore all too often subjective, which may account for the numerous variations in reported incidence. Overall, the reported incidence of secondary PPH in the developed world varies from 0.47% to 1.44%[2,3].

The etiology of secondary PPH is diverse, and management is dependent on identifying the cause and tailoring treatment appropriately (Table 1). In contrast to primary PPH, the published work on the management of secondary PPH is limited[4]. However, with declining maternal mortality rates in many parts of the world, interest in and attention to maternal morbidity and the important topic of management of secondary PPH is increasing. The majority of cases are associated with minor morbidities but may still require re-admission to hospital, use of antibiotics and surgical intervention. In more extreme cases, major morbidity may require hysterectomy, arterial ligation or radiological intervention[5]. Despite the use of all available interventions, maternal death may still result from massive secondary PPH.

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Subinvolution/uterine atony

The major cause of secondary PPH is uterine subinvolution (Table 1). Distinction should be made between the use of this term to describe the finding of a uterine fundus that is not resolving toward its pre-pregnancy size and the histological condition of failure of obliteration of blood vessels underlying the placental site, the latter leading to prolonged bleeding (see Chapter 22)[6]. One recent case report of a maternal death due to hemorrhage 8 days postpartum confirmed a failure of subinvolution of the uteroplacental arteries with large, dilated spiral arteries in the superficial myometrium at the placental implantation site containing partially occluding thrombi[7]. The main causes of this are infection, inflammation (endometritis) and retained placental tissue. Endometritis is more common following prolonged rupture of membranes, prolonged labor, emergency cesarean section or with a retained placenta that had required manual removal. A history of offensive lochia, maternal pyrexia and uterine tenderness is often present, and retained placental tissue is more common in women with a previous history of retained placenta or if there were concerns at the time of delivery of incomplete placenta and/or membranes. The condition is less likely following delivery by cesarean section (Table 2). Differentiation between the two causes is often difficult and both conditions may coexist.

Lower genital tract trauma

Missed vaginal lacerations and hematomas may present as secondary PPH. These are often associated with traumatic deliveries or those requiring ventouse or forceps. Both usually present within the first few days after delivery. Infected suture lines and episiotomy sites may lead to wound breakdown and result in excessive vaginal bleeding.

Placental abnormalities

Placenta accreta, increta and percreta are all known causes of massive primary PPH. When managed conservatively with placental tissue left *in situ* (with or without methotrexate therapy), they can also be associated with delayed bleeding and the need for hysterectomy[8,9] (see Section 5).

Uterine abnormalities

Fibroids usually are associated with primary PPH. They cause uterine enlargement and prevent uterine involution, therefore leading to prolonged bleeding from the placental bed. More rarely, they can be associated with secondary PPH. Fibroids have usually been identified by ultrasound in the antenatal period.

Vascular abnormalities

Abnormalities of uterine vasculature such as arteriovenous malformations and false aneurysms may also lead to secondary PPH. Arteriovenous malformations are due to an abnormal communication between an artery and vein with proliferation of each vessel with interconnecting fistulae. It is believed these malformations may result from venous sinuses becoming incorporated in scars within the myometrium after necrosis of the chorionic villi. The majority are acquired after pregnancy and may result from trophoblastic disease, previous uterine curettage, uterine or cervical malignancy[10,11] or cesarean section[12–15] (see Chapter 26). In particular, there should be a high index of suspicion of uterine artery pseudoaneurysm in women presenting with secondary PPH after cesarean section[16]. Diagnosis can be delayed for a considerable time, with one report describing a case of uterine artery pseudoaneurysm presenting 99 days after cesarean section[17]. Diagnosis is usually made using ultrasound with color Doppler analysis, angiography or computed tomography (CT).

Cesarean section wound dehiscence or surgical injury

Injury to pelvic blood vessels at the time of cesarean section[14] usually presents within 24 h. However, later presentations, in particular those causing broad ligament hematomas, have been described[5] and should be considered in women presenting acutely with signs of intra-abdominal hemorrhage. Delayed presentation of bleeding from non-union/dehiscence of the cesarean section uterine scar has also been described. This is believed to be due to local infection at the site of uterine closure causing erosion of blood vessels. In the cases reported, this led to massive PPH 2–3 weeks after cesarean section and the need for subtotal hysterectomy[18]. Diagnosis of uterine dehiscence postcesarean section associated with infection has also been made at hysteroscopy[19], although causing less significant PPH and only requiring treatment with antibiotics.

Table 1 Causes of secondary PPH

Subinvolution of the uterus – retained placental tissue and/or endometritis, fibroid uterus
Lower genital tract lacerations/hematoma
Surgical injury
Dehiscence of cesarean section scar
Vascular abnormality – arteriovenous malformation
Placental abnormality – placenta accreta, percreta and increta
Choriocarcinoma
Coagulopathies, bleeding disorders, use of anticoagulants

Choriocarcinoma

The majority of cases of choriocarcinoma after a non-molar pregnancy present with secondary PPH or irregular vaginal bleeding[20]. In addition, secondary symptoms of metastatic disease may be present. The diagnosis is made by evaluation of serum human chorionic gonadotropin (hCG) levels, histological findings and radiological imaging including ultrasound, plain film X-ray and CT scan.

Bleeding disorders, coagulopathies and use of anticoagulants

Women with congenital hemorrhagic disorders such as von Willebrand's disease (quantitative or qualitative deficiency of von Willebrand factor), carriers of hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency) and factor XI deficiency are at an increased risk of PPH. Often, these abnormalities are undetected until challenged by trauma, surgery or childbirth and thus may be undiagnosed prior to pregnancy. These women are not at increased risk of antepartum hemorrhage[21], but are at significant risk of both primary and secondary PPH with the risk of secondary PPH being greater than primary as the pregnancy-induced rise in maternal clotting factors falls after delivery.

The reported incidence for secondary PPH in these conditions is 20–28% for von Willebrand's disease, 11% for hemophilia carriers and 24% in factor XI deficiency[22–25]. Postpartum acquired hemophilia has also been described. This is a rare condition but can cause severe hemorrhage. It is caused by antibodies to factor VIII which partially or completely suppress factor VIII procoagulant activity in women with previously normal levels and activity of factor VIII. Bleeding usually commences within 3 months of delivery but may be delayed for up to 12 months[21]. The use of anticoagulants in the postpartum period may also cause delayed bleeding. In particular, women using warfarin should be carefully monitored and informed of the risks of hemorrhage.

Table 2 Risk factors for secondary PPH[4]

Pre-existing risk factors	*Antepartum risk factors*	*Intrapartum risk factors*	*Postpartum risk factors*
Maternal smoking at the time the antenatal history is taken	Prelabor rupture of membranes at term	Delivery by cesarean section	Primary postpartum hemorrhage
A previous history of secondary PPH	Threatened miscarriage	Precipitate labor of less than 2 hours	Not breastfeeding
Multiparous women	Multiple pregnancy	Prolonged third stage	Postnatal sepsis
	Antepartum hemorrhage	Incomplete placenta or membranes passed at birth, or both	
	Hospital admission during the third trimester		

MANAGEMENT OF SECONDARY POSTPARTUM HEMORRHAGE

Evidence regarding the management of secondary PPH is limited. A Cochrane review assessed all randomized or quasi-randomized comparisons of drug, surgical and placebo therapies or no treatment for secondary PPH. Forty-five papers were identified, but none met the inclusion criteria, and the review concluded there was no evidence from randomized trials to show the effects of treatments for secondary PPH[4]. The main aims of treatment are to provide basic resuscitation, establish a cause for the bleeding, and tailor the treatment (medical and/or surgical) according to the cause.

Resuscitation

Approximately 10% of cases present with massive hemorrhage[26] and require immediate attention. In these instances, resuscitation should be commenced prior to establishing a cause and should include the involvement of senior staff at the earliest opportunity. Restoration of circulating blood volume should be achieved by gaining intravenous access with two large-bore cannulae and administering intravenous fluids initially with physiological saline (up to 2 liters) and then with plasma expanders until blood is available. *There is considerable discussion in the recent literature that restoration of lost volume with plasma expanders delays the use of blood and that when necessary uncrossmatched blood but preferably type specific (Rh negative) can be used or O negative blood (see Chapter 4).* Blood should be obtained for full blood count, coagulation screen and crossmatch. High concentration oxygen (10–15 l/min) should be administered by a tight-fitting mask[27]. Close observation of vital signs including pulse, blood pressure, oxygen saturation and urine output should be maintained throughout resuscitation. *Blood and blood products should be given according to blood loss, rather than waiting and using the response to initial fluid administration and hemoglobin and coagulation results as the trigger for the infusion of blood.* Identification of the cause of bleeding should then be made and further management planned accordingly. In cases of less significant hemorrhage, basic resuscitation should be instigated as appropriate but blood transfusion should not be delayed whilst establishing a cause for the bleeding.

Clinical presentation

Ninety-five per cent of women with secondary PPH present within the first month after delivery, 19% within 7 days, 41% in 8–14 days, 23% in 15–21 days and 12% in 22–28 days[2]. The amount of blood loss at presentation varies but most patients are hemodynamically stable. A thorough history provides information relating to cause and should include details regarding parity, labor, mode of delivery, third-stage or puerperal complications and any relevant medical and family history.

Clinical signs and symptoms at the time of presentation may include offensive lochia, abdominal cramping, uterine tenderness, pyrexia, enlarged uterus and an open cervical os. Normal postpartum loss may continue beyond 6 weeks in up to 25% of women, especially if breastfeeding[26], and the first period may be heavy, prolonged and painful as a result of an anovulatory cycle. Women should be given this information during normal postpartum care to avoid unnecessary concern and presentation for medical investigation.

Investigations

Baseline blood tests should include full blood count, coagulation studies, C-reactive protein, a group and hold specimen, and serum hCG. Vaginal swabs should be taken at the time of examination for aerobic as well as anaerobic bacterial growth, including swabs from episiotomy or vaginal tear sites. In women with signs of infection, a mid-stream urine specimen should be collected and, if maternal temperature is more than 38°C, blood cultures should be obtained.

Ultrasound imaging of the pelvis should be considered if there are concerns of retained placental tissue. If this is obtained within 7–14 days of delivery, interpretation may be difficult as remaining blood clots may appear as mixed echogenic material in a similar manner to retained tissue. The use of duplex color Doppler helps to improve diagnostic accuracy in differentiating clot and tissue[28], as retained placental tissue will often maintain a blood supply unlike necrotic decidua and clot[29].

The over-diagnosis of retained placental tissue on ultrasound may lead to unnecessary surgical intervention and its potential complications. However, ultrasound does have significant benefits, as it has a good negative predictive value and therefore is helpful in excluding a diagnosis of retained placental tissue. Neill and colleagues assessed 53 women undergoing ultrasound for secondary PPH. Definitive diagnosis of retained placental tissue was made either histologically or, in those women managed conservatively, absence of retained tissue was assumed if bleeding diminished within 1 week. In their hands, ultrasound assessment had a positive predictive value of 46% (95% confidence interval (CI) 31–70%), a negative predictive value of 96% (95% CI 88–100%), with a sensitivity of 93% (95% CI 80–100%) and a specificity of 62% (95% CI 48–79%)[30] (Table 3).

This study also suggested that a standardized approach to reporting an ultrasound investigation of secondary PPH would be helpful. This is shown in Table 3. Additional imaging should also be considered for specific causes of secondary PPH such as plain chest film and CT scanning for metastases in cases of choriocarcinoma, magnetic resonance imaging (MRI) for placenta accreta[31,32] and angiography for intractable bleeding of unknown origin[14].

Treatment

The majority of cases of secondary PPH are due to subinvolution of the uterus caused by uterine infection and/or retained placental tissue. Initial management should include resuscitation as discussed above, the use of uterotonic agents, administration of antibiotics and consideration of surgical evacuation (Table 4).

Uterotonic agents

Syntocinon® can be administered as an intravenous or intramuscular bolus (10 units) or in combination with ergometrine (Syntometrine®) 1 ampoule as an intramuscular injection. This can be followed by a Syntocinon infusion (40 units in 500 ml normal saline at an infusion rate of 125 ml/h). Prostaglandin F2α (Haemabate®/carboprost) can be given by intramuscular injection at a dose of 250 μg every 15 min, up to a total of 2 mg (i.e. 8 doses). Misoprostol can also be given as an alternative prostaglandin (400–800 μg orally or rectally).

Antibiotics

Endometritis is likely to play a significant role in many cases of secondary PPH, and the majority of women are prescribed antibiotics. In a 3-year study of almost 20,000 women, 132 women (0.69%) had a secondary PPH, and 97% of these were treated with antibiotics[2]. However, only 75% of these women had microbiological specimens collected; of these, a positive culture was obtained in only 13.5%. In a similar observational study of 83 women, 45% presented with pyrexia and 64 had bacteriological swabs taken, of which only 12.5% were positive. Organisms identified included group B streptococcus, *Bacteroides sp.*, *Escherichia coli*, *Clostridium perfringens* and group D streptococcus. Despite the lack of evidence to support the presence of a specific bacterial pathogen, 92% of the women received antibiotics[3]. Recommended choices of antibiotic treatment include amoxicillin with clavulanic acid (Augmentin®)[33] and a combination of amoxycillin, metronidazole and gentamicin[3]. Endometritis is a major contributor to subinvolution of the uterus. Although infection may not be confirmed in a large population of cases, we recommend that antibiotics are always given for secondary PPH.

Table 3 A proposed standardized system for reporting postpartum ultrasound scan. Adapted from Neill *et al.*, 2002[30]

1. Normal endometrial cavity
2. Endometrial cavity containing fluid only
3. Endometrial cavity enlarged (anteroposterior (AP) depth >1 cm). Maximum AP dimensions noted
4. Endometrial cavity containing echogenic foci. Dimensions of largest foci noted. Doppler evaluation of blood flow in foci

Table 4 The management of secondary PPH

Medical	*Surgical*
Oxytocics	Uterine evacuation
Prostaglandins	Uterine tamponade balloon
Antibiotics	Uterine compression sutures
Tranexamic acid	Hysterectomy
Vasopressin	Pelvic arterial ligation
Clotting factor concentrates	
Chemotherapy	*Radiological*
Oral contraceptive pill	Selective arterial embolization

Uterine evacuation

Examination under anesthetic and surgical evacuation of the uterus should be considered if retained placental tissue is suspected clinically or after ultrasound examination. This intervention has good reported success rates, with bleeding stopping promptly in all 72 women undergoing evacuation of the uterus for secondary PPH in one study, despite only 36% having proven histological evidence of retained tissue[3]. However, this study was unable to find any clear association with presence or absence of retained tissue at the time of evacuation and day of onset of bleeding or other morbidity at the time of secondary PPH. Nonetheless, retained tissue was more likely if membranes were incomplete at delivery, primary PPH had occurred or if secondary PPH was judged to be heavy or moderate (compared with light) in volume.

The use of ultrasound prior to surgical evacuation of the uterus does not appear to significantly alter the chances of histological diagnosis confirming retained tissue. In one study, 33% of those with no preoperative scan had retained placental tissue compared to 37% following a scan[2]. Retained placental tissue is likely to be associated with infection and, therefore, broad spectrum intravenous antibiotics should be given in conjunction with surgical evacuation. As serum concentrations of most antibiotics peak 1 h after intravenous administration, these should be administered just prior to surgery[26]; in women who are hemodynamically stable, however, it may be appropriate to administer 12–24 h of antibiotic cover prior to surgery[1]. At the time of surgery, uterotonic agents such as Syntocinon, ergometrine and prostaglandins may be helpful to aid uterine contractility and control hemorrhage. There is no clear evidence to support which method of evacuation should be used. Manual removal of tissue, use of a suction catheter and sharp curettage with a metal curette have all been described[2]. The risk of uterine perforation is much higher in postpartum uterine evacuation and may be even further increased if associated with endometritis. Hoveyda and colleagues describe uterine perforation in three of 85 women undergoing evacuation for secondary PPH. Procedures were performed from 4 days to 28 days after delivery with both a suction and metal curette. In all cases, operations were performed by senior medical staff. One woman went on to require a hysterectomy, but the two others were managed conservatively[2].

Perforation after cesarean section is more likely and, as these women have a lower risk of retained placental tissue, surgical evacuation in such instances should be considered very carefully. An additional complication

is the risk of Asherman's syndrome. Limited evidence is available to ascertain whether this risk is increased for postpartum uterine evacuation; however, in a large study of intrauterine adhesions, 21.5% of cases had a postpartum curettage as a prior event[34]. The need for a second procedure due to incomplete evacuation of retained tissue may also occur[2]. Hysterectomy may be required to control bleeding in up to 5% of cases[26]. In view of these significant complications, women should always be fully counseled of the risks and informed consent obtained. Surgery should be performed by experienced senior medical staff.

Other surgical procedures

In the event of a large bleed, other surgical procedures should be considered. These include cases of bleeding from an infected placental bed or placental abnormality such as placenta accreta, bleeding from retained placental tissue not controlled with uterine evacuation, non-union/dehiscence of cesarean section scar, bleeding from a surgical injury or uncontrolled bleeding from a lower genital tract laceration. All are discussed in detail in other chapters of this book as is the insertion of an intrauterine tamponade balloon, such as the Bakri[35] or Rüsch balloon[36], which may be considered in cases of secondary PPH due to uterine subinvolution/atony once retained placental tissue has been excluded. Laparotomy may also be required which allows further investigation into the cause of bleeding and treatment by the use of surgical compression sutures, hysterectomy and pelvic arterial ligation as appropriate. The B-Lynch brace suture is well described for the treatment of primary PPH[37] and has now been reported in hundreds of cases of secondary PPH (B-Lynch, personal communication). The use of a surgical compression suture may avoid the need for hysterectomy in women wishing to conserve fertility (see Chapters 44, 47 and 48 for balloons and Chapter 51 for compression sutures).

Within an Australian population with an overall incidence of secondary PPH of 1.44% over 15 years, only nine cases required hysterectomy (0.9%)[3]. However, in a subgroup of women with massive intractable obstetric hemorrhage, two out of seven with secondary PPH required hysterectomy. In one, hysterectomy was performed 7 days after delivery due to intractable bleeding from lower genital tract lacerations but maternal death still resulted. *[Editor's note: It is possible that, as discussed in the first chapter of the book, hysterectomy might not have been the operation of choice given the fact that the bleeding came from vaginal lacerations. L.G.K.]* The second case had further morbidity following her hysterectomy for secondary PPH with bleeding from wound disunion and sepsis; she required bilateral hypogastric artery ligation 14 days after delivery[5].

Hysterectomy in cases of PPH carries significant risks but can be life-saving and should be considered early rather than late in cases of massive hemorrhage, whether primary or secondary. If delayed, patients may already be in shock, have disseminated intravascular coagulopathy (DIC) or acidosis, all of which add significantly to the operation's risk and may contribute to its failure as does its use in patients where the bleeding is not from arteries that perfuse the uterus but rather from those which supply blood to the lower uterine segment and the upper vagina (see Chapter 1).

Pelvic artery ligation may also be considered for cases of massive secondary PPH uncontrolled by medical and simple surgical measures. Lédée and colleagues report the use of bilateral hypogastric artery ligation in 49 of 61 cases of intractable hemorrhage; this includes four out of seven cases of secondary PPH, all of which were successful at arresting bleeding[5] (see Chapter 52) As with primary PPH, arterial ligation should be performed by an experienced surgeon and their involvement should be considered early whilst planning a laparotomy in such cases.

Bilateral uterine artery embolization and selective arterial embolization

Pelvic angiography to assess the internal iliac artery, uterine artery and its vaginal branches is a helpful tool in the assessment of ongoing hemorrhage. It also allows the introduction of embolization agents to arrest bleeding. Pelage and colleagues studied 14 women presenting with uncontrollable secondary PPH at a mean of 16 days after delivery[14]. Six women (43%) had delivered by cesarean section and the remainder by spontaneous vaginal delivery. Eight women exhibited evidence of endometritis (57%), four with histologically proven retained placental tissue; a further four women had genital tract lacerations, and the remaining two had no obvious cause for bleeding. Basic resuscitation with use of medical treatments and/or uterine curettage was performed. Angiography found no extravasation in eight women, active bleeding in three women from uterine and vaginal vessels, a false uterine artery aneurysm in two women, and evidence of an arteriovenous fistula in another. Pledgets of absorbable gelatin sponge were introduced to embolize the uterine arteries bilaterally in 12 women. Unilateral embolization of a false aneurysm and an arteriovenous fistula was performed for the other two women. External bleeding disappeared immediately, and hemodynamic stability and correction of coagulopathy were obtained for all cases. There were no general or local complications[14]. Ganguli *et al.* reported a clinical success rate for secondary PPH of 88% with uterine artery embolization[16].

One of the authors of this chapter (T.J.) managed a case of massive secondary PPH presenting 4 days after a cesarean section. An emergency subtotal hysterectomy was performed with good initial results. Two hours later, vaginal bleeding restarted. There was no evidence of significant coagulopathy. Pelvic angiography was performed and a bleed from a false aneurysm related to a middle branch of the anterior division of the left internal iliac artery was identified (Figure 1). The vessels were embolized with four coils. There was immediate cessation of bleeding and the

patient's vital signs normalized (Figure 2). The patient made a good recovery despite requiring 24 units of blood during the hemorrhage. Subsequent histology of the uterus showed acute inflammation and subinvolution of the placental bed.

Other measures

In cases of massive hemorrhage unsuccessfully treated with surgical measures, the use of intravenous tranexamic acid[38–41], recombinant factor VIIa[42] and local vasopressin[43] have been reported for primary PPH. There are no reports of similar use in secondary PPH but, if available, it may be appropriate to consider their use in combination with other therapies and resuscitative support. A trial currently underway may provide further information in the future[44].

Chemotherapy

The mainstay of treatment for choriocarcinoma is chemotherapy. A low-risk chemotherapy regimen includes the use of methotrexate with folinic acid rescue on a 2-weekly cycle[45]. Medium- and high-risk regimens include the use of etopside, methotrexate, actinomycin, vincristine, cyclophosphomide and 6-mercaptopurine[46,47]. Women with choriocarcinoma are most appropriately treated through specialist trophoblastic disease referral centers[20].

Coagulopathies

Women with inherited coagulation disorders such as von Willebrand's disease and carriers of hemophilia A and B are likely to bleed postpartum if maternal clotting factors are low (<50 IU/dl). Prophylactic administration of desmopressin (DDAVP) and clotting factor concentrates may prevent PPH[21]. The aim is to raise factor levels above 50 IU/dl during labor and delivery, and to maintain these for up to 5 days after delivery. In the event of PPH, replacement of deficient clotting factors should be made and identification and treatment of the cause be instigated. Management should be in close liaison with hematologists and specialist hemophilia centers as available (see Chapter 25). In cases of prolonged or intermittent secondary PPH, the use of tranexamic acid (a fibrinolytic inhibitor)[48] or combined oral contraceptive pill has been reported[22]. Hemorrhage from postpartum acquired hemophilia is treated acutely with factor VIII (human or porcine) or recombinant factor VIIa[21]. Immunosuppressive drugs such as corticosteroids, cyclophosphamide and azathioprine may be used to accelerate the disappearance of factor VIII inhibitors, although complete remission is likely to occur spontaneously with time. Reversal of bleeding due to anticoagulants should follow normal protocols. Vitamin K should be considered in women with uncontrolled bleeding secondary to warfarin use and protamine sulfate may be considered if hemorrhage results from the use of heparin, although this has a much shorter half-life.

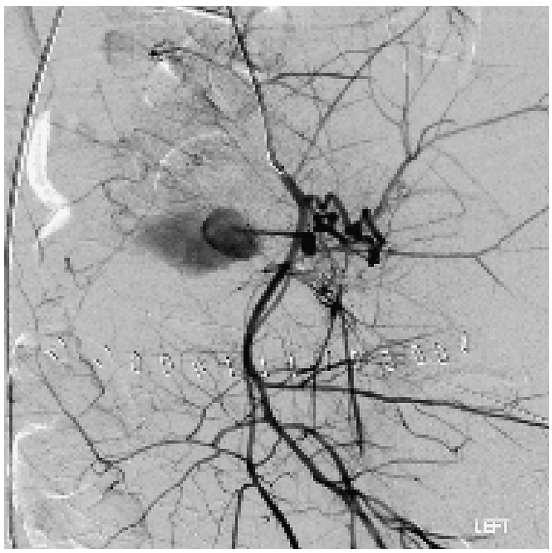

Figure 1 Angiogram demonstrating brisk hemorrhage from false aneurysm prior to embolization

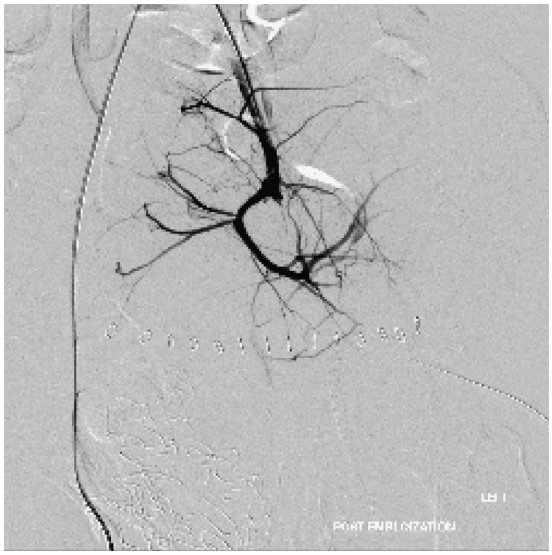

Figure 2 Angiogram after embolization

CONCLUSION

Secondary PPH is an important cause of maternal morbidity and mortality. Basic resuscitation followed by investigation and treatment of the specific cause of hemorrhage are essential. The diverse nature of its etiology and often acute presentation make research in the form of randomized controlled trials difficult. However, particularly for the treatment of hemorrhage due to uterine infection and/or retained placental tissue, this should be achievable and would provide valuable information to further our understanding of the management of secondary PPH.

References

1. Thompson W, Harper M. Postpartum haemorrhage and abnormalities of the third stage of labour. In: Chamberlain G, Steer P, eds. Turnbull's Obstetrics, 3rd edn. Edinburgh: Churchill Livingstone, 2001:619–33

2. Hoveyda F, MacKenzie IZ. Secondary postpartum haemorrhage: incidence, morbidity and current management. BJOG 2001;108:927–30
3. King PA, Duthie SJ, Dong ZG, Ma HK. Secondary postpartum haemorrhage. Aust N Z J Obstet Gynaecol 1989;29: 394–8
4. Alexander J, Thomas PW, Sanghera J. Treatments for secondary postpartum haemorrhage (Review). Cochrane Database Syst Rev 2008;(1): http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002867/frame.html
5. Ledee N, Ville Y, Musset D, Mercier F, Frydman R, Fernandez H. Management in intractable obstetric haemorrhage: an audit study on 61 cases. Eur J Obstet Gynecol Reprod Biol 2001;94:189–96
6. Babarinsa IA, Hayman RG, Draycott TJ. Secondary postpartum haemorrhage: challenges in evidence-based causes and management. Eur J Obstet Gynecol Reprod Biol 2011;159: 255–60
7. Farley NJ. Kohlmeier RE. A death due to subinvolution of the uteroplacental arteries. J Forensic Sci 2011;56:803–5
8. Matthews NM, McCowan LM, Patten P. Placenta praevia accreta with delayed hysterectomy. Aust N Z J Obstet Gynaecol 1996;36:476–9
9. Jaffe R, DuBeshter B, Sherer DM, Thompson EA, Woods JR Jr. Failure of methotrexate treatment for term placenta percreta. Am J Obstet Gynecol 1994;171:558–9
10. Ghosh TK. Arteriovenous malformation of the uterus and pelvis. Obstet Gynecol 1986;68:40S–3S
11. Gaylis H, Levine E, van Dongen LG, Katz I. Arteriovenous fistulas after gynecologic operations. Surg Gynecol Obstet 1973;137:655–8
12. Bardou P, Orabona M, Vincelot A, Maubon A, Nathan N. [Uterine artery false aneurysm after caesarean delivery: an uncommon cause of post-partum haemorrhage]. Ann Fr Anesth Reanim 2010;29:909–12
13. Bhatt A, Odujebe O, Bhatt S, Houry D. Uterine artery pseudoaneurysm rupture: a life-threatening presentation of vaginal bleeding. Ann Emerg Med 2010;55:460–3
14. Pelage JP, Soyer P, Repiquet D, et al. Secondary postpartum hemorrhage: treatment with selective arterial embolization. Radiology 1999;212:385–9
15. Kelly SM, Belli AM, Campbell S. Arteriovenous malformation of the uterus associated with secondary postpartum hemorrhage. Ultrasound Obstet Gynecol 2003;21:602–5
16. Ganguli S, Stecker MS, Pyne D, Baum RA, Fan CM. Uterine artery embolization in the treatment of postpartum uterine hemorrhage. J Vasc Interv Radiol 2011;22:169–76
17. Isono W, Tsutsumi R, Wada-Hiraike O, et al. Uterine artery pseudoaneurysm after cesarean section: case report and literature review. J Minim Invasive Gynecol 2010;17:687–91
18. Nanda S, Singhal S, Sharma D, Sood M, Singhal SK. Nonunion of uterine incision: a rare cause of secondary postpartum haemorrhage: a report of 2 cases. Aust N Z J Obstet Gynaecol 1997;37:475–6
19. Paraskevaides E, Stuart B, Gardeil F. Secondary postpartum haemorrhage from nondehisced lower caesarean section scar: a case for hysteroscopy. Aust N Z J Obstet Gynaecol 1993;33: 427
20. Tidy JA, Rustin GJ, Newlands ES, et al. Presentation and management of choriocarcinoma after nonmolar pregnancy. Br J Obstet Gynaecol 1995;102:715–9
21. Economides DL, Kadir RA, Lee CA. Inherited bleeding disorders in obstetrics and gynaecology. Br J Obstet Gynaecol 1999;106:5–13
22. Kadir RA, Economides DL, Braithwaite J, Goldman E, Lee CA. The obstetric experience of carriers of haemophilia. Br J Obstet Gynaecol 1997;104:803–10
23. Greer IA, Lowe GD, Walker JJ, Forbes CD. Haemorrhagic problems in obstetrics and gynaecology in patients with congenital coagulopathies. Br J Obstet Gynaecol 1991;98:909–18
24. Ramsahoye BH, Davies SV, Dasani H, Pearson JF. Obstetric management in von Willebrand's disease: a report of 24 pregnancies and a reivesw of the literature. Haemophilia 1995;1:140–4
25. Kadir RA, Lee CA, Sabin CA, Pollard D, Economides DL. Pregnancy in women with von Willebrand's disease or factor XI deficiency. Br J Obstet Gynaecol 1998;105:314–21
26. Neill A, Thornton S. Secondary postpartum haemorrhage. J Obstet Gynaecol 2002;22:119–22
27. Johanson R, Cox C, O'Donnell E, Grady K, Howell C, Jones P. Managing obstetric emergencies and trauma (MOET): Structured skills training using models and reality-based scenarios. Obstetrician Gynaecologist 1999;1:46–52
28. Achiron R, Goldenberg M, Lipitz S, Mashiach S. Transvaginal duplex Doppler ultrasonography in bleeding patients suspected of having residual trophoblastic tissue. Obstet Gynecol 1993;81:507–11
29. Zuckerman J, Levine D, McNicholas MM, et al. Imaging of pelvic postpartum complications. Am J Roentgenol 1997; 168:663–8
30. Neill AC, Nixon RM, Thornton S. A comparison of clinical assessment with ultrasound in the management of secondary postpartum haemorrhage. Eur J Obstet Gynecol Reprod Biol 2002;104:113–5
31. Thorp Jr JM, Wells SR, Wiest HH, Jeffries L, Lyles E. First-trimester diagnosis of placenta previa percreta by magnetic resonance imaging. Am J Obstet Gynecol 1998; 178:616–8
32. Levine D, Barnes PD, Edelman RR. Obstetric MR Imaging. Radiology 1999;211:609–17
33. Fernandez H, Claquin C, Guibert M, Papiernik E. Suspected postpartum endometritis: a controlled clinical trial of single-agent antibiotic therapy with Amox-CA (AugmentingR) vs. ampicillin-metronidazole ± aminoglycoside. Eur J Obstet GynecolReprod Biol 1990;36:69–74
34. Schenker JG, Margalioth EJ. Intrauterine adhesions: an updated appraisal. Fertil Steril 1982;37:593–610
35. Bakri YN, Amri A, Abdul Jabbar F. Tamponade-balloon for obstetrical bleeding. Int J Gynecol Obstet 2001;74:139–42
36. Johanson R, Kumar M, Obhrai M, Young P. Management of massive postpartum haemorrhage: use of a hydrostatic balloon catheter to avoid laparotomy. BJOG 2001;108:420–2
37. B-Lynch C, Coker A, Lawal AH, Abu J, Cowen MJ. The B-Lynch surgical technique for the control of massive postpartum haemorrhage: an alternative to hysterectomy? Five cases reported. Br J Obstet Gynaecol 1997;104:372–5
38. Alok K, Hagen P, Webb JB. Tranexamic acid in the management of postpartum haemorrhage. BJOG 1996;103:1250–1
39. Ducloy-Bouthors AS, Jude B, Duhamel A, et al. High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. Crit Care 2011;15:R117
40. Ferrer P, Roberts I, Sydenham E, Blackhall K, Shakur H. Anti-fibrinolytic agents in post partum haemorrhage: a systematic review. BMC Pregnancy Childbirth 2009;9:29
41. Novikova N, Hofmeyr GJ. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev 2010; (7):CD007872
42. Boehlen F, Morales MA, Fontana P, Ricou B, Irion O, de Moerloose P. Prolonged treatment of massive postpartum haemorrhage with recombinant factor VIIa: case report and review of the literature. BJOG 2004;111:284–7
43. Lurie S, Appleman Z, Katz Z. Subendometrial vasopressin to control intractable placental bleeding. Lancet 1997;349:698
44. Shakur H, Elbourne D, Gulmezoglu M, et al. The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. Trials 2010;11:40
45. Bagshawe KD, Dent J, Newlands ES, Begent RHJ, Rustin GJS. The role of low-dose methotrexate and folinic acid in gestational trophoblastic tumours (GTT). BJOG 1989;96: 795–802
46. Newlands ES, Bagshawe KD, Begent RHJ, Rustin GJS, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine)

regimen in high risk gestational trophoblastic tumours, 1979 to 1989. BJOG 1991;98:550–7
47. Rustin GJ, Newlands ES, Begent RH, Dent J, Bagshawe KD. Weekly alternating etoposide, methotrexate, and actinomycin/vincristine and cyclophosphamide chemotherapy for the treatment of CNS metastases of choriocarcinoma. J Clin Oncol 1989;7:900–3
48. Bonnar J, Guillebaud J, Kasonde JM, Sheppard BL. Clinical applications of fibrinolytic inhibition in gynaecology. J Clin Pathol Suppl (R Coll Pathol) 1980;14:55–9