1	Management of Retained Products of Conception with Marked Vascularity
2	
3	Tomoko Kitahara, Yukiyasu Sato*, Kazuyo Kakui, Keiji Tatsumi, Hiroshi Fujiwara, and
4	Ikuo Konishi
5	
6	Department of Gynecology and Obstetrics, Kyoto University Graduate School of
7	Medicine
8	
9	*Address correspondence and reprint requests to: Yukiyasu Sato, M.D., Ph.D.
10	Department of Gynecology and Obstetrics, Kyoto University Graduate School of
11	Medicine, Sakyo-ku, Kyoto 606-8507, Japan.
12	Tel; 81-75-751-3269: Fax; 81-75-761-3967: E-mail; yukiyasu@kuhp.kyoto-u.ac.jp
13	
14	Short title; Management of Hypervascular RPOC
15	Keywords; color Doppler, uterine artery embolization, expectant management
16	

1 Abstract

2

3 Cases of retained products of conception (RPOC) with marked vascularity present a 4 clinical challenge because simple dilation and curettage (D&C) can lead to 5 life-threatening hemorrhage. We describe here two cases of hypervascular RPOC that 6 were successfully managed with two different approaches.

Case 1: A 26-year-old woman with history of 3 D&C's was transported to the emergency room for heavy vaginal bleeding 45 days after the spontaneous abortion. Diagnosis of RPOC with aneurysm-like structure was considered and uterine artery embolization (UAE) was performed. Four days after the UAE, reduction of the vascularity of RPOC was confirmed on color Doppler ultrasonography and D&C was successfully carried out.

13 Case 2: A 37-year-old woman with history of 1 cesarean section became pregnant 14 after the regular menses. She underwent D&C for missed abortion at 8 weeks' 15 gestation. Seven days after the D&C, sonographically heterogenous mass emerged in 16 the vicinity of the previous cesarean scar. Thereafter, the mass gradually grew larger 17 and diagnosis of hypervascular placental polyp was considered. As the amount of 18 vaginal bleeding was small, expectant management was instituted. Sixty-one days 19 after the first D&C, reduction of the vascularity of RPOC was confirmed on color 20 Doppler ultrasonography and D&C was successfully completed.

1 Introduction

2 Retained product of conception (RPOC) is defined as a portion of placental tissue that 3 remained in the uterine cavity after abortion or term delivery. RPOCs are estimated to 4 occur after approximately 1% of term pregnancies and probably more often after spontaneous or induced abortion 1 . The retention of placental tissue is suspected in the 5 case of persistent postpartum or post-abortion uterine bleeding with mildly to 6 7 moderately elevated serum hCG. Hyperechoic endometrial mass is the most sensitive 8 and specific sonographic feature of RPOC². The diagnosis requires histopathological 9 examination of the evacuated tissue 3,4 .

10 The introduction of color Doppler ultrasonography has allowed evaluation of blood 11 supply to RPOC. Several cases of RPOC with prominent vascularity have been These include hypervascular placental polyp, which is defined as 12 published. 13 intrauterine mass formed by fibrin deposition around degenerated retained placental 14 tissue, with prominent vascularity and RPOC mimicking arteriovenous malformations⁵ 15 ⁶⁻¹⁰. These hypervascular RPOCs present a clinical challenge, because simple D&C 16 could lead to life-threatening hemorrhage. Indeed, invasive treatment such as uterine 17 artery embolization (UAE) or hysterectomy was performed in most of these cases.

According to a recent report, nearly 20% of RPOCs had marked vascularity ¹¹, which 18 19 are more common than previously thought. Timmerman et al. assessed spontaneous 20 outcome of 30 cases of uterine vascular malformation that is defined as an abnormal hypervascular area with turbulent flow in the myometrium on color Doppler imaging ¹². 21 22 Remarkably, expectant management was successful in more than two-thirds of the cases, 23 raising the possibility that expectant management is an appropriate option in many of 24 the cases of uterine hypervascular lesion. Although intramyometrial peak systolic 25 velocities tended to be lower in the cases that were treated expectantly as compared 26 with those required UAE, the difference was not statistically significant ¹². For the 27 present, there is no reliable measure to predict future spontaneous massive hemorrhage 28 from the uterine hypervascular lesion.

Here, we report two cases of hypervascular RPOC that were successfully managedwith two different approaches.

- 1 Case Report
- 2
- 3 Case 1

4 A 26-year-old woman (gravida 4, para 1: artificial abortion 2, spontaneous abortion 1, 5 vaginal delivery 1) with history of 3 dilations and curettages (D&C's) consulted our hospital for lower abdominal pain with small amount of vaginal bleeding. 6 7 Transvaginal ultrasonography (TV-USG) showed gestational sac (GS) of 6.9 mm in 8 lower part of the uterine cavity (Figure 1A). The day after, she spontaneously passed 9 chorionic tissue followed by relief of the lower abdominal pain. When she revisited 10 our hospital 7 days after the spontaneous passage, GS was no longer detected on 11 TV-USG. Vaginal bleeding was markedly decreased but still continued intermittently.

12 She was transported to the emergency room due to repetitive heavy vaginal bleeding 13 45 days after the spontaneous passage. On arrival, vaginal bleeding subsided and her 14 vital condition was stable with hemoglobin level of 12.4 g/dl. TV-USG showed round 15 heterogenous mass in the lower uterine segment, which contained anechoic space with 16 brisk color Doppler blood inflow from the right uterine artery (Figure 1B). Spectral 17 Doppler analysis demonstrated the presence of low-impedance arterial flow with peak 18 systolic velocity of 70 cm/s (Figure 1C). Moderate color Doppler flow in the rim of 19 the mass (Figure 1B) combined with mildly elevated serum hCG (142 mIU/ml) 20 suggested the retention of chorionic tissue. From these findings, the diagnosis of 21 retained product of conception (RPOC) with aneurysm-like structure was considered.

Magnetic resonance imaging (MRI) also revealed round mass with heterogenous intensity in T2-weighed MRI (Figure 1D) and relatively low intensity in T1-weighed MRI (Figure 1E), which was considered to reflect blood of various time courses. In gadolinium-contrasted T1-weighed MRI, the anterior portion (aneurysm-like structure) and the posterior rim (retained chorionic tissue) of the mass were markedly enhanced (Figure 1F).

Removal of RPOC was considered to be necessary to prevent relapse of heavy vaginal bleeding. Since immediate D&C could cause intractable hemorrhage, bilateral uterine artery embolization (UAE) using gelatin sponge was performed on the same day. The angiography performed prior to UAE revealed tortuous dilated uterine artery flowing into sac-like structure (Figure 2A). The day after, anechoic space with brisk color Doppler flow disappeared (Figure 2B). The patient suffered from uterine cramping pain for a few days, which necessitated opioid analgesics. Four days after the UAE, her serum hCG level declined to 31.5 mIU/mL and D&C was successfully carried out. Seven days after the D&C, no apparent retention or abnormal power Doppler flow was detected in the lower uterine segment (Figure 2C). Degenerated chorionic villi were microscopically found in the evacuated tissue and the diagnosis of RPOC was confirmed. Her serum hCG fell below measurable limits 39 days after and her menstrual cycle resumed 56 days after the D&C.

8

9 Case 2

10 A 37-year-old woman (gravida 1, para 1) with history of 1 low transverse cesarean 11 section at 28 weeks of gestation for premature rupture of membrane became pregnant 12 after regular menses. TV-USG at 8 weeks of gestation showed GS of 25.8 mm in 13 relatively lower part of the uterine cavity (Figure 3A). Cesarean scar ectopic 14 pregnancy was unlikely because GS did not directly contact with the previous cesarean 15 scar. D&C was carried out under the diagnosis of missed abortion. Her serum hCG level prior to D&C was 88,847 mIU/mL. No retention was detectable in the uterine 16 17 cavity immediately after the procedure (Figure 3B). Seven days after D&C, 18 sonographically heterogenous mass of 2 cm emerged in the vicinity of the previous 19 cesarean scar (Figure 3C), although her serum hCG declined to 9,407 mIU/mL. 20 Thirteen days after D&C, the mass grew to 3 cm. Gestational trophoblastic disease was 21 unlikely because her serum hCG level further declined to 3,408 mIU/mL. T2-weighed 22 MRI revealed that round mass of heterogenous intensity in the lower uterine segment 23 with extremely thinned previous cesarean scar (Figure 3D). Magnetic resonance 24 angiography showed prominent vascularization in the mass (Figure 3E). Development 25 of hypervascular placental polyp was considered and she was referred to our hospital 28 26 days after D&C. Small amount of vaginal bleeding was continued after D&C, but no 27 other remarkable symptom was noted.

28 At her first examination, amount of vaginal bleeding was scanty and her vital

29 condition was stable with hemoglobin level of 12.6 g/dl. TV-USG showed

30 pear-shaped heterogenous mass in the lower uterine segment, which had further grew to

31 5 cm. No color Doppler flow was detected inside the mass, indicating that vascularity

32 of the placental polyp had been spontaneously reduced. However, brisk color Doppler

33 flow was still observed at the boundary between the mass and the surrounding

1 myometrium. Spectral Doppler analysis demonstrated the presence of low-impedance 2 arterial flow with peak systolic velocity of 27 cm/s (Figure 4B). Moderately elevated 3 serum hCG (384 mIU/mL) suggested the retention of chorionic tissue and the diagnosis-4 of hypervascular placental polyp was considered. Since her vaginal bleeding was only 5 scanty amount and immediate D&C could cause intractable hemorrhage, expectant 6 management with oral methylergometrine maleate was instituted, anticipating possible 7 reduction of the blood supply and eventual spontaneous passage of the placental polyp. 8 She was thoroughly informed of the possibility for spontaneous massive vaginal 9 bleeding and referred to interventional radiologist in preparation for potential 10 emergency UAE. Small amount of vaginal bleeding intermittently continued 11 throughout the waiting period, which was well tolerated. Sixty-one days after D&C, 12 her serum hCG level declined to 1.12 mIU/ml and power Doppler flow towards the 13 placental polyp became undetectable (Figure 4C). The placental polyp shrunk to 3 cm, 14 but the spontaneous passage seemed unlikely because of tightly closed uterine cervix. 15 Thus, the second D&C was performed under USG guidance not to perforate the 16 previous cesarean scar. Some difficulty was encountered in removing the polyp from 17 the previous cesarean scar. The day after, no apparent retention was observed on 18 TV-USG (Figure 4D). Ghost cell-like trophoblasts were microscopically found in the 19 evacuated tissue and the diagnosis of placental polyp was confirmed. Her serum hCG fell below measurable limits 17 days after and her menstrual cycle resumed 54 days 20 21 after the removal of the placental polyp. 22

1 Discussion

2

3 Excessive myometrial invasion by trophobalsts could be one of the causes for 4 prolonged retention of chorionic tissue in the uterus after removal of the conceptus. In 5 this situation, physiological maternal arteriovenous shunting in the placental bed could 6 persist and even expand, leading to the development of retained product of conception 7 (RPOC) with prominent vascularity. In this respect, excessive trophoblast invasion 8 could be one of the underlying etiologies for hypervascular RPOC. On the other hand, 9 it is well known that excessive trophoblast invasion is also the primary basis of the 10 development of placenta accreta late in pregnancy. Accordingly, reported risk factors for placenta accreta such as prior cesarean deliveries and history of multiple D&Cs^{13,14} 11 12 could also be the predisposing factors for the development of hypervascular RPOC. 13 Moreover, since endometrium is thin and decidual formation tends to be insufficient in 14 lower part of the uterus, embryo implantation in this part could induce excessive 15 trophoblast invasion, which might be one of the reasons for the association between 16 placenta previa and accreta. Interestingly, embryo implantation occurred in relatively 17 lower part of the uterus in both of our cases. Moreover, history of 3 D&C's was noted 18 in case 1 and prior cesarean section in case 2. Thus, both of our cases carried high risk 19 for exaggerated trophoblast invasion that could lead to the development of 20 hypervascular RPOC. In fact, some difficulty was encountered in removing the 21 placental polyp from the previous cesarean scar in case 2.

22 Evaluation of the vascularity is important to determine treatment strategy for RPOC, 23 because simple D&C against hypervascular RPOC can lead to intractable bleeding that 24 may necessitate life-saving hysterectomy. Thus, we took stepwise treatment approach 25 to hypervascular RPOC. First, we tried to reduce the blood supply to RPOC either by 26 uterine arterial embolization (UAE) in case 1 or prolonged expectant management in 27 case 2. At the present time, there is no reliable measure to predict future spontaneous 28 massive hemorrhage and expectant management with or without uterotonics might be 29 preferable to invasive UAE as long as the vaginal bleeding is mild and the patient is hemodynamically stable ^{15, 16}. In the case of expectant management, however, patient 30 31 should be informed of possibility for spontaneous massive hemorrhage that may require 32 emergency UAE or, at worst, hysterectomy. After the blood supply became nearly 33 undetectable on color Doppler ultrasonography, D&C was performed in both of our 1 cases, although spontaneous passage of RPOC has been reported ^{9, 11, 16}. In case 1, 2 D&C was performed 4 days after UAE for fear of possible recurrence of aneurysm-like 3 structure after recanalization of the uterine artery that had been temporarily occluded 4 with gelatin sponge. In case 2, we waited for 2 months but it appeared that relatively 5 large size of the placental polyp and tightly closed uterine cervix hampered the 6 spontaneous passage.

In conclusion, simple D&C of hypervascular RPOC should be deferred until its vascularity is sufficiently reduced. Since there is currently no reliable measure to predict future spontaneous massive hemorrhage, expectant management may be preferable to emergency UAE as long as the condition of patients allows. Future studies should characterize hypervascular RPOC that causes spontaneous heavy bleeding and not eligible for expectant management.

5
5

-	
3	[1] Romero R, Hsu YC, Athanassiadis AP, <i>et al.</i> Preterm delivery: a risk factor
4	for retained placenta. Am J Obstet Gynecol. 1990; 163(3): 823-5.
5	[2] Durfee SM, Frates MC, Luong A, Benson CB. The sonographic and color
6	Doppler features of retained products of conception. J Ultrasound Med. 2005; 24(9):
7	1181-6; quiz 8-9.
8	[3] Hertzberg BS, Bowie JD. Ultrasound of the postpartum uterus. Prediction of
9	retained placental tissue. J Ultrasound Med. 1991; 10(8): 451-6.
10	[4] Abbasi S, Jamal A, Eslamian L, Marsousi V. Role of clinical and ultrasound
11	findings in the diagnosis of retained products of conception. Ultrasound Obstet Gynecol.
12	2008; 32 (5): 704-7.
13	[5] Takeuchi K, Ichimura H, Masuda Y, Yamada T, Nakago S, Maruo T.
14	Selective transarterial embolization and hysteroscopic removal of a placental polyp with
15	preservation of reproductive capacity. J Reprod Med. 2002; 47(8): 608-10.
16	[6] Kido A, Togashi K, Koyama T, <i>et al</i> . Retained products of conception
17	masquerading as acquired arteriovenous malformation. J Comput Assist Tomogr. 2003;
18	27 (1): 88-92.
19	[7] Ichikawa Y, Nakauchi T, Sato T, Oki A, Tsunoda H, Yoshikawa H.
20	Ultrasound diagnosis of uterine arteriovenous fistula associated with placental site
21	trophoblastic tumor. Ultrasound Obstet Gynecol. 2003; 21(6): 606-8.
22	[8] Kelly SM, Belli AM, Campbell S. Arteriovenous malformation of the uterus
23	associated with secondary postpartum hemorrhage. Ultrasound Obstet Gynecol. 2003;
24	21 (6): 602-5.
25	[9] Jain K, Fogata M. Retained products of conception mimicking a large
26	endometrial AVM: complete resolution following spontaneous abortion. J Clin
27	Ultrasound. 2007; 35 (1): 42-7.
28	[10] Takeda A, Koyama K, Imoto S, Mori M, Sakai K, Nakamura H. Placental
29	polyp with prominent neovascularization. Fertil Steril. 2009.
30	[11] Kamaya A, Petrovitch I, Chen B, Frederick CE, Jeffrey RB. Retained
31	products of conception: spectrum of color Doppler findings. J Ultrasound Med. 2009;
32	28 (8): 1031-41.

- 1 [12] Timmerman D, Wauters J, Van Calenbergh S, et al. Color Doppler imaging is
- 2 a valuable tool for the diagnosis and management of uterine vascular malformations.
- 3 *Ultrasound Obstet Gynecol.* 2003; **21**(6): 570-7.
- 4 [13] Ota Y, Watanabe H, Fukasawa I, *et al.* Placenta accreta/increta. Review of 10
 5 cases and a case report. *Arch Gynecol Obstet.* 1999; **263**(1-2): 69-72.
- 6 [14] Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year
- 7 analysis. *Am J Obstet Gynecol*. 2005; **192**(5): 1458-61.
- 8 [15] Timmerman D, Van den Bosch T, Peeraer K, et al. Vascular malformations in
- 9 the uterus: ultrasonographic diagnosis and conservative management. *Eur J Obstet*
- 10 *Gynecol Reprod Biol.* 2000; **92**(1): 171-8.
- 11 [16] Dar P, Karmin I, Einstein MH. Arteriovenous malformations of the uterus:
- 12 long-term follow-up. *Gynecol Obstet Invest*. 2008; **66**(3): 157-61.

1 Figure Legend

2

3 Figure 1. Ultrasonographic and magnetic resonance images before uterine arterial 4 embolization in case 1. (A) Transvaginal gray-scale ultrasonogram shows gestational 5 sac in lower part of the uterine cavity, which spontaneously passed through vagina the 6 next day. (B) Transvaginal color Doppler ultrasonogram 45 days after the spontaneous 7 tissue passage shows emergence of round heterogenous mass in lower part of the uterine 8 cavity that contains anechoic space with brisk color Doppler blood flow, indicating the 9 formation of aneurysm-like structure. Note moderate color Doppler flow in the rim of 10 the mass (arrows) that represents retained chorionic tissue. (C) Spectral Doppler 11 analysis on the blood flow into aneurysm-like structure reveals low-impedance arterial 12 waveform with peak systolic velocity of 70 cm/s. (D) T2-weighed magnetic resonance 13 image shows heterogenous-intensity round mass (arrow). (E) In T1-weighed magnetic 14 resonance image, the mass shows relatively low intensity representing blood of different 15 ages. (F) Gadolinium (Gd)-contrasted T1-weighed MRI shows marked enhancement in 16 the anterior portion (aneurysm-like structure, closed arrow) and the posterior rim 17 (retained chorionic tissue, open arrow) of the mass.

18

19 Figure 2. Angiographic and ultrasonographic images before and after uterine arterial 20 embolization (UAE) in case 1. (A) Angiography performed before UAE reveals 21 tortuous dilated uterine artery (arrow) flowing into sac-like structure (arrowhead). (B) 22 Transvaginal color Doppler ultrasonogram 1 day after UAE shows complete 23 disappearance of the aneurysm-like structure in the mass (arrow). Four days after 24 UAE, the avascular mass was safely removed with dilation and curettage (D&C). (C) 25 Transvaginal power Doppler ultrasonogram 7 days after D&C shows no detectable 26 retention in lower part of the uterine cavity (arrow).

27

Figure 3. Ultrasonographic and magnetic resonance images before referral to our hospital in case 2. (A) Transvaginal gray-scale ultrasonogram before dilation and curettage (D&C) shows gestational sac in lower part of the uterine cavity. (B) Transvaginal gray-scale ultrasonogram immediate after D&C shows no detectable intrauterine retention. (C) Transvaginal gray-scale ultrasonogram 7 days after D&C shows emergence of heterogenous round mass in lower part of the uterine cavity indicating the formation of placental polyp. (D) T2-weighed magnetic resonance
 image 13 days after D&C shows heterogenous-intensity placental polyp in the vicinity
 of thinned previous cesarean scar (arrowhead). (E) Magnetic resonance angiography
 (MRA) 13 days after D&C shows prominent vascularization (arrow) in the placental
 polyp.

6

7 Figure 4. Ultrasonographic images after referral to our hospital in case 2. (A) 8 Transvaginal color Doppler ultrasonogram 28 days after dilation and curretage (D&C) 9 shows pear-shaped heterogenous placental polyp (broken line) with brisk color Doppler 10 blood flow (arrow), indicating the presence of feeding vessel. (B) Spectral Doppler 11 analysis on the feeding vessel reveals low-impedance arterial waveform with peak 12 systolic velocity of 27 cm/s. (C) Transvaginal color Doppler ultrasonogram 61 days 13 after D&C shows disappearance of power Doppler flow towards the placental polyp and 14 the avascular placental polyp was safely removed with the second D&C. (D) 15 Transvaginal gray-scale ultrasonogram 1 day after the second D&C shows no detectable 16 retention in the uterine cavity.

Figure 1





(E)



(F)



Figure 2



(B)



(C)



Figure 3



(D)

(E)





Figure 4







(D)

