Ethanol Embolotherapy of Pelvic Arteriovenous Malformations: an Initial Experience

Sooho Bae, MD[1]
Young Soo Do, MD[1]
Sung Wook Shin, MD[1]
Kwang Bo Park, MD[1]
Dong-Ik Kim, MD[2]
Young Wook Kim, MD[2]
Sung Ki Cho, MD[1]
Sung Wook Choo, MD[1]
In Wook Choo, MD[1]

Objective: We retrospectively assessed the results of performing ethanol embolization for pelvis arteriovenous malformations (AVMs).

Materials and Methods: During the past 10 years, eight patients (8 females, age range: 27–52 years) with AVMs in the pelvic wall (n = 3) and uterus (n = 5) underwent staged ethanol embolizations (range: 1–5, mean: 2.5) under general anesthesia. Ethanol embolization was performed by the use of the transcatheter and/or direct puncture techniques. Clinical follow-up was performed for all of the patients, and imaging follow-up was available for seven patients. The therapeutic outcomes were established by evaluating the clinical outcome of the signs and symptoms, as well as the degree of devascularization observed on post-procedural angiography.

Results: During the 20 sessions of ethanol embolization, the solitary transarterial approach was used 14 times, the transvenous approach was used three times and direct puncture was used once. For two patients, the transarterial and transvenous or direct puncture approaches were used together in one session. For four patients, ethanol and coils were used as embolic agents, and n-butyl cyanoacrylate (NBCA) and ethanol were used in one patient. Seven (88%) of eight patients were cured of their AVMs and one patient (12%) displayed improvement. Major complications were seen in two patients (25%).

Conclusion: Ethanol embolization is effective for the treatment of pelvic arteriovenous malformations, though there is a chance of a major complication.

Index terms:
Arteriovenous malformation
Embolism, therpeutic
Interventional procedures

DOI:10.3348/kjr.2008.9.2.148

Korean J Radiol 2008;9:148-154
Received March 2, 2007; accepted after revision June 27, 2007.

[1]Department of Radiology and Center for Imaging Science, [2]Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 135-710, Korea

Address reprint requests to:
Young Soo Do, MD, Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Korea.
Tel. (822) 3410-0515
Fax. (822) 3410-2559
e-mail: ysdo@smc.samsung.co.kr

Among the many kinds of arteriovenous malformations (AVMs), the pelvis AVM is especially difficult to diagnose because of its scarcity, vague symptoms and its deep location. The pelvis AVM is a potentially life-threatening disease due to the potential for spontaneous hemorrhage and congestive heart failure (1).

Surgical treatment, the classic method for treating vascular malformations, including pelvic AVMs, either by ligation of the afferent arteries or by attempted excisions, has not usually been successful as surgical eradication of the nidus of an AVM is rarely possible. Further, this is often followed by recurrence and progression of the disease (2, 3). Selective embolization can obliterate AVMs and it is increasingly being employed for the treatment of pelvic AVMs. Although intra-arterial embolization of AVMs by using particulate materials can provide symptomatic relief, the lesions recur in most cases because the nidus is not permanently occluded (4, 5). Superselective catheterization or direct puncture of the nidus and the use of ethanol as a permanent embolic agent have shown good clinical and radiological implications for improving the treatment of AVMs, with an acceptable risk of morbidity (5, 6).

The purpose of this study is to assess retrospectively the results of performing ethanol embolization of pelvis AVMs.

MATERIALS AND METHODS

Patients

We obtained institutional review board approval at our hospital for conducting a retrospective review of patient medical and imaging records. Written consent for the procedure was obtained from all the patients after a discussion about the advantages and risks of the procedure. From November 1996 to March 2006, we performed staged ethanol embolization on eight female patients with AVMs in the pelvic wall and uterus. The mean age of the patients was 35.9 years (age range: 27−52 years). One patient had a history 10 years prior of a previous dilatation and curettage following a recurrent abortion, and this was suggestive of a traumatic AVM. The AVMs in seven patients were considered to be of a congenital origin. For all the patients except one, who had previously undergone unsuccessful embolizations with microcoils and particles at another institution, ethanol embolization was decided to be used as a primary treatment by the consensus of gynecologic surgeons, vascular surgeons and interventional radiologists after conducting a full review of the findings from the clinical and radiological examinations of the patients. The patients displayed various signs and symptoms: vaginal bleeding (3 of 8 patients) and pain (2 of 8 patients) were the most common signs and symptoms. One patient had cardiomegaly and a recurrent abortion and another patient had dysmenorrhea. In one patient, an incidental pelvic mass was detected on routine pelvic ultrasonography. Five patients had AVMs in the uterus and three had AVMs in the pelvic wall. Imaging studies including the use of Doppler ultrasound (US), computed tomography (CT) or CT angiography, magnetic resonance imaging (MRI) with gadolinium contrast or the gradient echo sequence, and technetium 99m-labeled red blood cell scintigraphy were first used for making a diagnosis, and then selective angiography was performed to define accurately the feeding arteries, draining veins and nidus of the AVMs.

Procedure

All of the procedures were performed under general anesthesia. A Swan-Ganz catheter (Baxter Healthcare, Irvine, CA) was inserted for the pulmonary arterial monitoring that preceded the embolization procedure. If an elevation of the mean pulmonary arterial pressure (> 25 mmHg) was detected, then nitroglycerine was administered as a bolus injection (50−100 μg) and then it was continuously infused at 0.3−3.0 ($\mu g - kg^{-1}$)/min through the Swan-Ganz catheter until the mean pulmonary artery pressure reached normal levels.

Staged ethanol embolization was performed to embolize all or part of the nidus. The routes for gaining vascular access to the nidus were chosen after performance of initial angiography. Transarterial catheterization, transvenous catheterization by using a coaxial microcatheter for the superselection of the nidus and/or direct percutaneous puncture were required to reach the nidus itself and not the vascular feeders for embolization (5). An additional balloon catheter was used to reduce proximal flow to the nidus when ethanol was injected in two sessions for two patients. Pure (99.9%) ethanol was used as an embolic agent. The amount of ethanol used was based on the amount of contrast medium required to fill the AVM nidus without opacifying the normal vessels. During the 20 sessions of ethanol embolization, the solitary transarterial approach was used 14 times, the transvenous approach was used three times and direct puncture was used once. In two patients, the transarterial and transvenous or direct puncture approaches were used together in one session (Fig. 2). In 6 sessions of four cases with multiple feeders and a dominant draining vein, coils (Nester coil; Cook, Bloomington, IN) were used to reduce the amount of required ethanol in the nidus of the AVM and to stabilize the thrombosis in the dilated outflow vein as previously reported (5). In one case, n-butyl cyanoacrylate (NBCA) was additionally used with ethanol to stop vaginal bleeding.

To control the localized soft tissue swelling in the pelvic wall and uterus, a corticosteroid (0.1 mg/kg dexamethasone, Dexamethasone, Yuhan, Seoul, Korea), was given immediately before the procedure and then every eight hours intravenously by bolus injection while the patients were in the hospital (5, 7). After the patients were discharged, prednisolone (Solondo; Yuhan) was administered orally at 1 $mg - kg^{-1}$)/d (maximum daily dose, 15 mg) in three divided doses, which was tapered over a 1-week period. Any hemoglobinuria that occurred during the procedure was managed by means of hydration with an intravenously administered crystalloid solution. To evaluate renal function, serum creatinine and urea levels were measured at least once during the hospital stay.

Evaluation of the Clinical Data and Follow-up Results

Two radiologists working in consensus analyzed the therapeutic responses to ethanol embolization by comparing the degree of AVM devascularization between the baseline angiography and final angiography (i.e., 100%,

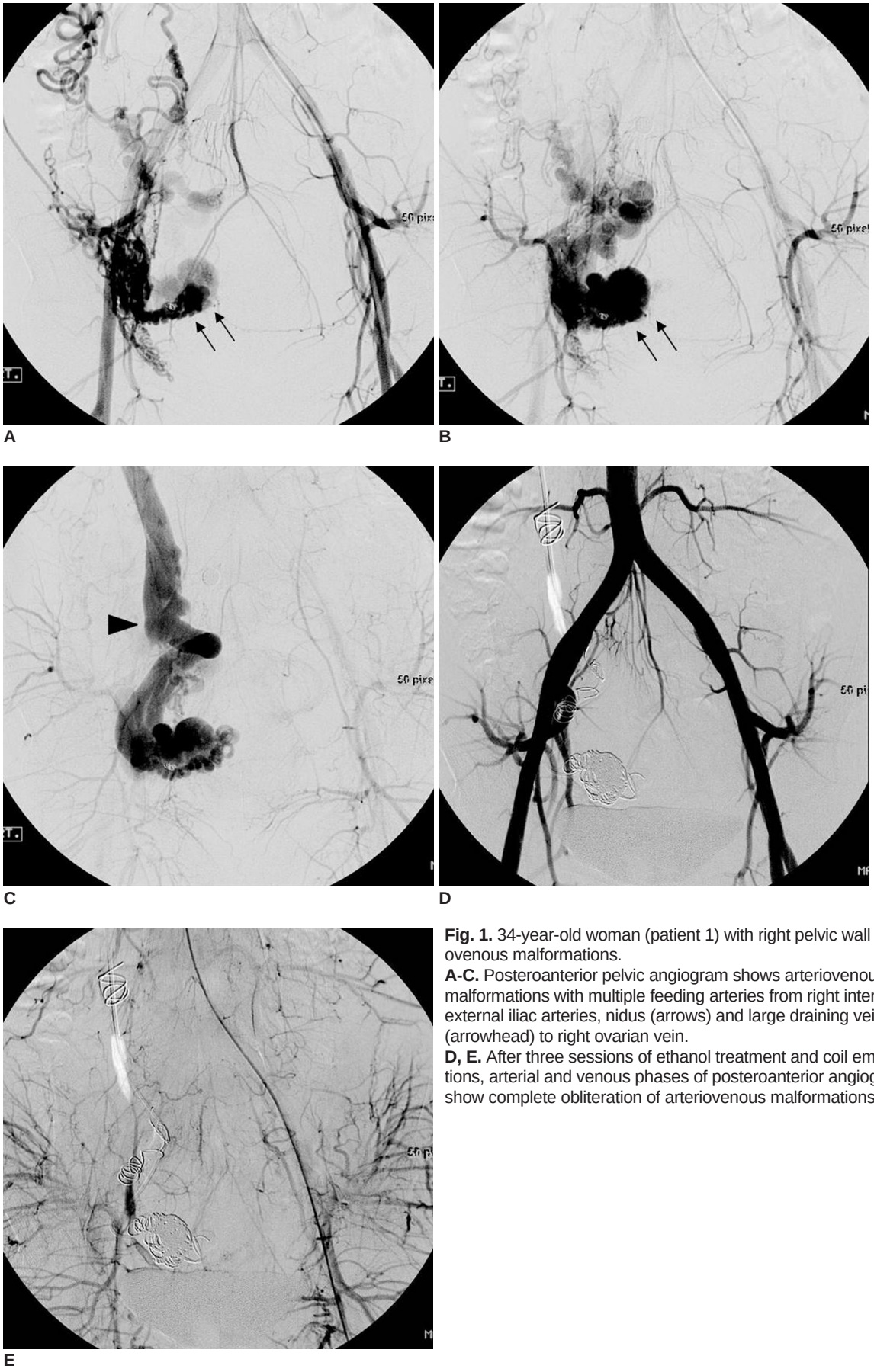

Fig. 1. 34-year-old woman (patient 1) with right pelvic wall arteriovenous malformations.
A-C. Posteroanterior pelvic angiogram shows arteriovenous malformations with multiple feeding arteries from right internal and external iliac arteries, nidus (arrows) and large draining vein (arrowhead) to right ovarian vein.
D, E. After three sessions of ethanol treatment and coil embolizations, arterial and venous phases of posteroanterior angiogram show complete obliteration of arteriovenous malformations.

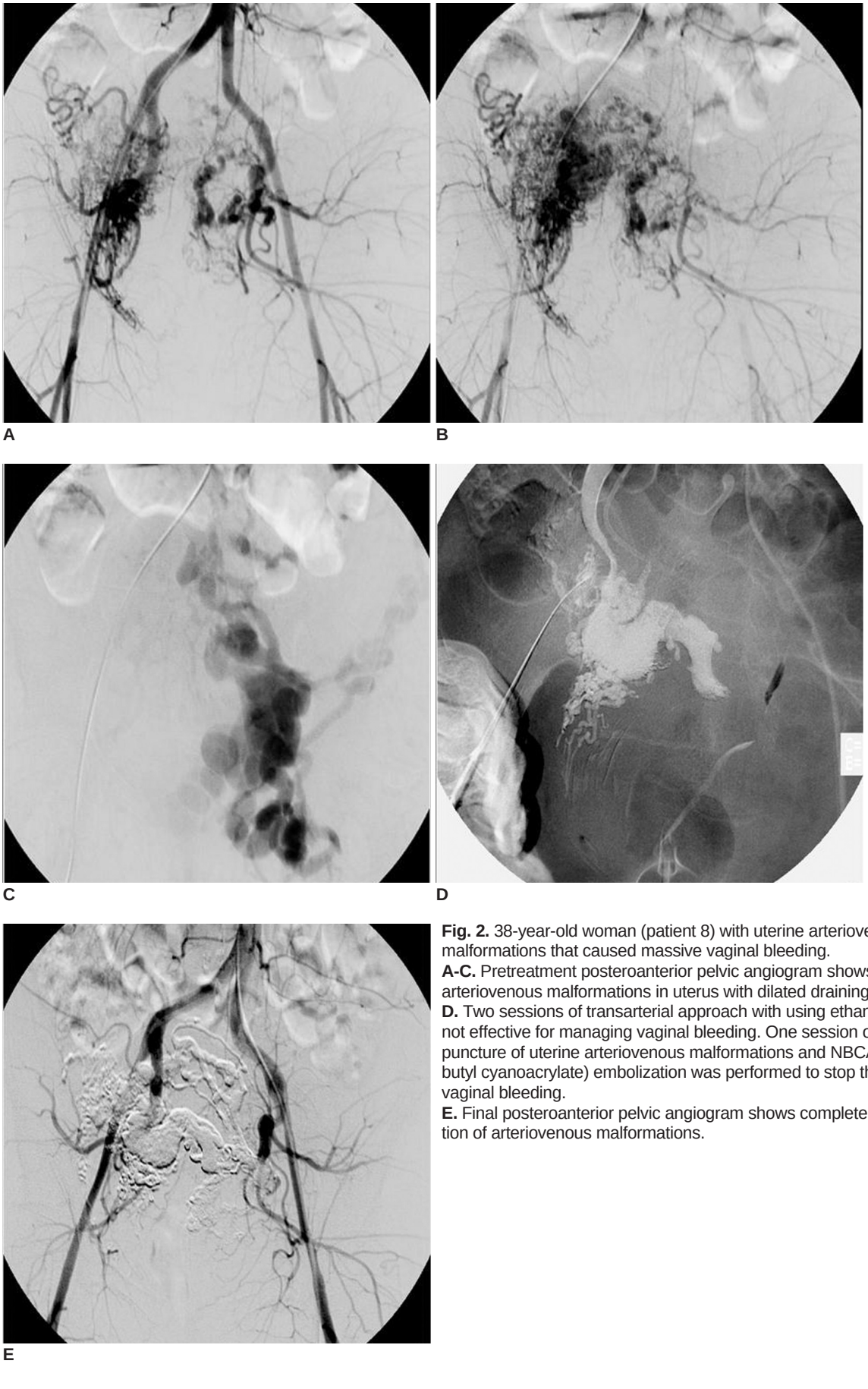

Fig. 2. 38-year-old woman (patient 8) with uterine arteriovenous malformations that caused massive vaginal bleeding.
A-C. Pretreatment posteroanterior pelvic angiogram shows large arteriovenous malformations in uterus with dilated draining veins.
D. Two sessions of transarterial approach with using ethanol were not effective for managing vaginal bleeding. One session of direct puncture of uterine arteriovenous malformations and NBCA (n-butyl cyanoacrylate) embolization was performed to stop the vaginal bleeding.
E. Final posteroanterior pelvic angiogram shows complete obliteration of arteriovenous malformations.

76−99%, 50−75%, or < 50%). The clinical outcome of the signs and symptoms (complete or partial resolution, no change, or aggravation) was evaluated at the congenital vascular malformation clinic by a consensus of two surgeons and one interventional radiologist. Cure was defined as complete resolution of the signs and symptoms, and 100% devascularization of the AVMs being observed by angiography. Improvement was defined as complete or partial resolution of the signs and symptoms, and 50−99% devascularization of the AVMs observed on angiography. No change was defined as partial resolution or no change of the signs and symptoms, and less than 50% devascularization of the AVMs observed on angiography. Cure and improvement were considered effective therapeutic outcomes of ethanol embolization.

Complications were classified as being either major or minor. The major complications included death, permanent adverse sequelae, the required performance of major therapy and prolonged hospitalization (> 48 hours). Minor complications included any nonpermanent adverse sequelae. The patients were physically and neurologically examined before and after embolization to assess the complications. When major complications were observed, we then reviewed the angiograms again to find the possible causes of the major complications.

Periodic (1−6 months) follow-up evaluation was performed based on the use of color Doppler US, technetium 99m-labeled red blood cell scintigraphy, CT or MRI during the multi-session therapy. Follow-up imaging (range: 14−82 months, median: 29 months) was available from the last treatment session for seven patients.

RESULTS

During the 20 sessions of ethanol embolizations (range: 1−5, mean 2.5), the amount of ethanol used ranged from 8 to 59 ml (mean: 30.3 ml) in a single embolization session. None of the patients experienced ethanol toxicity.

Seven (87.5%) patients were cured and one patient (12.5%) had improvement of the AVMs (Fig. 1). Ethanol embolization was considered an effective treatment for all the cases. Except for one patient, the AVMs were totally devascularized, as was demonstrated on the follow-up imaging studies. One patient who achieved improvement did not want further treatment. All the patients showed complete or partial resolution of their clinical symptoms and signs.

Two patients (25%) experienced major complications. One patient complained of urinary urgency after complete embolization of the pelvic AVMs. Focal bladder necrosis was confirmed upon cystoscopy and this healed after two weeks of conservative management. Another patient developed permanent ovarian insufficiency as a chronic complication after four sessions of ethanol embolization for treatment of uterine AVMs. Hormone replacement therapy was needed to improve the symptoms of ovarian insufficiency.

DISCUSSION

Pelvic AVMs can have either a congenital or an acquired etiology. Congenital AVMs are the result of anomalous differentiation or developmental arrest in the primitive capillary plexus during the 4th and 10th weeks of embryonic life, and they usually present at a young age. They tend to extend to the surrounding tissues beyond the uterus (6, 8−10). Acquired AVMs may develop due to dilatation and curettage (D & C), therapeutic abortion, surgery, cancer and gestational trophoblastic disease (GTD). As a distinction, acquired AVMs are usually confined to the uterus and they tend to have single or bilateral feeding arteries, no blood supply from the extrauterine arteries, the lack of a nidus and a single draining vein (10). Some investigators have suggested that acquired uterine AVMs are multiple small arteriovenous fistulae between the intramural arterial branches and the myometrial venous plexus, and they appear as a vascular tangle that mimics the congenital AVMs (11−13).

Surgical treatment of pelvic AVMs, either by ligation of the afferent arteries or by an attempted excision, has not usually been successful as surgical eradication of the nidus of an AVM is rarely possible and surgery is often followed by recurrence and progression of disease. Several investigators agree that simple ligation of the feeding artery is not effective since new collaterals rapidly develop to bypass the ligated vessels and most of the cases of surgical treatment reported in the literature have included a hysterectomy (2, 3, 6).

Transcatheter arterial embolization for uterine AVMs was originally used in the intraoperative setting to stop bleeding in women suffering with congenital AVMs. Especially in women that want to preserve their fertility, transcatheter arterial embolization has been proposed as a relatively safe technique (6). Several agents have been used, and these have been associated with a few problems such as recanalization and difficulty in controlling the level of occlusion (5). In a series of pelvic AVMs that were related to gestational trophoblastic disease, initial control of uterine hemorrhage was achieved in 11 of 14 patients with embolization that used PVA (polyvinyl alcohol) particles (150−500 μm): six patients required repeat embolotherapy (14). In another study that mainly used

glue, six of 15 patients required a repeat embolization for recurrent bleeding (10).

The use of ethanol has shown good results for the management of AVMs, and this technique has shown the ability to induce protein denaturation of the endothelial cells with subsequent vessel wall denudation and interruption, which results in the complete obliteration of the vessel lumen rather than just simple obstruction (5, 15–17). However, there are several complications with the use of ethanol for various mechanisms such as local tissue injury (skin swelling, necrosis, peripheral nerve palsies), renal tubular necrosis (renal insuffiency), thrombus formation (thrombophlebitis, pulmonary embolism), and pulmonary arterial spasm (systemic arterial hypotension, cardiac arrhythmia, cardiopulmonary collapse) (5, 15). The careful use of ethanol and routine monitoring of pulmonary arterial pressure are required of the interventional radiologist.

The use of ethanol has proved its efficacy in the management of peripheral AVMs (5, 16, 18, 19). For treating peripheral AVMs of 40 patients, ethanol embolization was effective in 27 patients (68%), and only one patient showed aggravation of their AVMs (5). In this study, seven patients were cured and one patient experienced improvement. To the best of our knowledge, this is the first series that has treated pelvic AVMs with ethanol, and the results are comparable with the previous studies that used other embolic materials. Coils and NBCA were also used as embolic agents in some treatment sessions (Fig. 2). These were mainly used to reduce the total amount of ethanol. As recommended previously, we tried not to exceed a maximum volume of ethanol during sclerotherapy of over 0.5–1.0 mL/kg in every single session (19, 20).

We attempted as much as possible to perform embolization by the transarterial approach. Yet, very tortuous vascularity or the presence of adjacent major arterial branches made it necessary to perform additional transvenous or percutaneous embolization (17). Some investigators have reported that arterial embolization was unnecessary because of the slow flow of the arterial system, which is composed of multiple plexus-form arterial tributaries (2). However, this transvenous technique may cause inadvertent occlusion of the normal venous drainage from surrounding tissues with resultant venous hypertension and deep vein thrombosis (21). The direct puncture technique is easier and simpler to employ than the other techniques. Other sclerosants such as coils or NBCA cannot be used by this method, and extravasation may occur.

In this study, there were two major complications of non-targeted embolization. One patient suffered from urinary urgency that developed after the procedure. Focal bladder necrosis was found by cystoscopy. The bladder necrosis improved with conservative management. Another 42-year-old patient experienced permanent ovarian insufficiency. Ovarian failure occurs in 1–14% of patients after they undergo uterine arterial embolization for the management of symptomatic uterine fibroids. This can be explained as ovarian failure is associated with a reduced ovarian capacity in women over 40 years and by a compromised blood supply via the utero-ovarian collateral circulation after uterine arterial embolization (22, 23). In order to prevent such an embolic complication, some investigators have recommend confirming the patency of the collateral artery before embolization and performing the procedure as selectively as possible (24–26).

There are some limitations in this study. First, even though our treatment results were good, the number of cases was small. Second, in most cases we used ethanol rather than another embolic agent such as NBCA. If we had treated a larger number of pelvic AVMs, then a comparative study with other embolic agents might have been necessary. Finally, this study was insufficient for the evaluation of such delicate issues as pregnancy after ethanol sclerotherapy.

In conclusion, a pelvic AVM is a silent and dangerous condition in some situations. Ethanol embolization is an effective treatment for pelvic AVMs with a high cure rate based on our experience. However, there is a chance of major complications with the use of ethanol. It is mandatory to perform long-term follow-up for patients and to accumulate more experience with this technique to lessen the complication rate.

References

1. Beller U, Rosen RJ, Beckman EM, Markoff G, Berenstein A. Congenital arteriovenous malformation of the female pelvis: a gynecologic perspective. *Am J Obstet Gynecol* 1988;159:1153-1160
2. Olcott CT, Newton TH, Stoney RJ, Ehrenfeld WK. Intra-arterial embolization in the management of arteriovenous malformations. *Surgery* 1976;79:3-12
3. Mitsuzaki K, Yamashita Y, Utsunomiya D, Sumi S, Ogata I, Takahashi M, et al. Balloon-occluded retrograde transvenous embolization of a pelvic arteriovenous malformation. *Cardiovasc Intervent Radiol* 1999;22:518-520
4. Palmaz JC, Newton TH, Reuter SR, Bookstein JJ. Particulate intraarterial embolization in pelvic arteriovenous malformations. *AJR Am J Roentgenol* 1981;137:117-122
5. Do YS, Yakes WF, Shin SW, Lee BB, Kim DI, Liu WC, et al. Ethanol embolization of arteriovenous malformations: interim results. *Radiology* 2005;235:674-682
6. Vedantham S, Goodwin SC, McLucas B, Mohr G. Uterine artery embolization: an underused method of controlling pelvic hemorrhage. *Am J Obstet Gynecol* 1997;176:938-948
7. Donnelly LF, Bisset GS 3rd, Adams DM. Marked acute tissue swelling following percutaneous sclerosis of low-flow vascular

malformations: a predictor of both prolonged recovery and therapeutic effect. *Pediatr Radiol* 2000;30:415-419
8. Vogelzang RL, Nemcek AA Jr, Skrtic Z, Gorrell J, Lurain JR. Uterine arteriovenous malformations: primary treatment with therapeutic embolization. *J Vasc Interv Radiol* 1991;2:517-522
9. Tanaka M, Iida K, Matsumoto S, Takeuchi T, Yamaguchi K, Nishimura Y, et al. A case of pelvic arteriovenous malformation in a male. *Int J Urol* 1999;6:374-376
10. Ghai S, Rajan DK, Asch MR, Muradali D, Simons ME, TerBrugge KG. Efficacy of embolization in traumatic uterine vascular malformations. *J Vasc Interv Radiol* 2003;14:1401-1408
11. Kwon JH, Kim GS. Obstetric iatrogenic arterial injuries of the uterus: diagnosis with US and treatment with transcatheter arterial embolization. *Radiographics* 2002;22:35-46
12. Majmudar B, Ghanee N, Horowitz IR, Graham D. Uterine arteriovenous malformation necessitating hysterectomy with bilateral salpingo-oophorectomy in a young pregnant patient. *Arch Pathol Lab Med* 1998;122:842-845
13. Manolitsas T, Hurley V, Gilford E. Uterine arteriovenous malformation—a rare cause of uterine haemorrhage. *Aust N Z J Obstet Gynaecol* 1994;34:197-199
14. Lim AK, Agarwal R, Seckl MJ, Newlands ES, Barrett NK, Mitchell AW. Embolization of bleeding residual uterine vascular malformations in patients with treated gestational trophoblastic tumors. *Radiology* 2002;222:640-644
15. Hammer FD, Boon LM, Mathurin P, Vanwijck RR. Ethanol sclerotherapy of venous malformations: evaluation of systemic ethanol contamination. *J Vasc Interv Radiol* 2001;12:595-600
16. Yakes WF, Luethke JM, Merland JJ, Rak KM, Slater DD, Hollis HW, et al. Ethanol embolization of arteriovenous fistulas: a primary mode of therapy. *J Vasc Interv Radiol* 1990;1:89-96
17. Cho SK, Do YS, Shin SW, Kim DI, Kim YW, Park KB, et al. Arteriovenous malformations of the body and extremities: analysis of therapeutic outcomes and approaches according to a modified angiographic classification. *J Endovasc Ther* 2006;13:527-538
18. Takebayashi S, Hosaka M, Ishizuka E, Hirokawa M, Matsui K. Arteriovenous malformations of the kidneys: ablation with alcohol. *AJR Am J Roentgenol* 1988;150:587-590
19. Yakes WF, Rossi P, Odink H. How I do it. Arteriovenous malformation management. *Cardiovasc Intervent Radiol* 1996;19:65-71
20. Shin BS, Do YS, Lee BB, Kim DI, Chung IS, Cho HS, et al. Multistage ethanol sclerotherapy of soft-tissue arteriovenous malformations: effect on pulmonary arterial pressure. *Radiology* 2005;235:1072-1077
21. Jackson JE, Mansfield AO, Allison DJ. Treatment of high-flow vascular malformations by venous embolization aided by flow occlusion techniques. *Cardiovasc Intervent Radiol* 1996;19:323-328
22. Hascalik S, Celik O, Sarac K, Hascalik M. Transient ovarian failure: a rare complication of uterine fibroid embolization. *Acta Obstet Gynecol Scand* 2004;83:682-685
23. Tropeano G, Di Stasi C, Litwicka K, Romano D, Draisci G, Mancuso S. Uterine artery embolization for fibroids does not have adverse effects on ovarian reserve in regularly cycling women younger than 40 years. *Fertil Steril* 2004;81:1055-1061
24. Porcu G, Roger V, Jacquier A, Mazouni C, Rojat-Habib MC, Girard G, et al. Uterus and bladder necrosis after uterine artery embolisation for postpartum haemorrhage. *BJOG* 2005;112:122-123
25. Marx M, Wack JP, Baker EL, Stevens SK, Barakos JA. Ovarian protection by occlusion of uteroovarian collateral vessels before uterine fibroid embolization. *J Vasc Interv Radiol* 2003;14:1329-1332
26. Wolanske KA, Gordon RL, Wilson MW, Kerlan RK Jr, LaBerge JM, Jacoby AF. Coil embolization of a tuboovarian anastomosis before uterine artery embolization to prevent nontarget particle embolization of the ovary. *J Vasc Interv Radiol* 2003;14:1333-1338