

# Embolization of High Flow Arteriovenous Malformations: Experience with Use of Superabsorbent Polymer Microspheres

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**PURPOSE:** To determine efficacy, safety, and requirements for adjunctive embolization or surgery in the treatment of symptomatic arteriovenous malformations (AVMs) with superabsorbent polymer microsphere (SAP-MS) particles.

**MATERIALS AND METHODS:** SAP-MS particles (sodium acrylate and vinyl alcohol copolymer) are nonbiodegradable spheres with a precisely calibrated diameter. SAP-MS particles swell by absorbing fluids and become soft and deformable. Twenty-five patients (16 men, nine women; mean age, 32 y; range 12–66 y) with symptomatic facial ( $n = 5$ ), upper- ( $n = 8$ ) and lower- ( $n = 12$ ) extremity AVMs were treated primarily ( $n = 23$ ) or preoperatively ( $n = 2$ ) by transarterial embolization (TAE) treatment with use of SAP-MS particles. Direct puncture embolization (DPE;  $n = 4$ ) and/or surgical intervention ( $n = 5$ ; ie, skin graft, resection, or amputation) were required. Surgical specimens from the resected ( $n = 2$ ) and the amputated ( $n = 2$ ) patients were evaluated histologically. Follow-up study, including clinical findings and imaging studies, was performed at intervals ranging from 3 months to 1 year. Clinical outcome was evaluated retrospectively, depending on the subjective improvement of symptoms and signs, according to the medical records.

**RESULTS:** Seventy-two TAEs (range, 1–11; mean, 2.8) and 12 DPEs (range, 1–3; mean, 2.4) were performed during the mean follow-up period of 38 months (range, 7–110 mo). Twenty patients (80%) experienced symptom improvement by embolotherapy alone ( $n = 17$ ) or in combination with surgery ( $n = 3$ ). One lip and two finger AVMs were totally removed by surgical excision or amputation after TAE treatment. In diffuse upper- ( $n = 1$ ) and lower- ( $n = 1$ ) extremity AVMs, the symptoms were uncontrolled. No nerve injury or skin necrosis was observed after TAE treatment with SAP-MS particles. Mucosal necrosis was induced by DPE with ethanol in one patient. Histologically, SAP-MS particles penetrated intralésional vessels and conformed to the vessel lumen, resulting in tight vessel occlusion. Minimal perivascular reaction was observed.

**CONCLUSION:** SAP-MS particles were used safely in TAE treatment of AVM. TAE treatment with use of SAP-MS particles was suitable for certain symptomatic AVMs, but diffuse AVMs remain a challenge and a combination of alternative methods will be necessary for further strategy.

**Index terms:** Arteriovenous malformations, embolization • Embolization agents

J Vasc Interv Radiol 2002; 13:1125–1133

**Abbreviations:** AV = arteriovenous, AVM = arteriovenous malformation, DPE = direct puncture embolization, DSA = digital subtraction angiography, LE-AVM = lower-extremity arteriovenous malformation, NBCA = n-butyl cyanoacrylate, PVA = polyvinyl alcohol, SAP-MS = superabsorbent polymer microsphere, TAE = transarterial embolization, UE-AVM = upper-extremity arteriovenous malformation,

SYMPTOMATIC vascular malformations are difficult to manage and treat.

Mulliken et al (1,2) classified vascular malformations into high-flow type,

such as arteriovenous malformation (AVM), and low-flow type, such as capillary, venous, lymphatic, and mixed malformation (1,2). High-flow AVMs are less common than low-flow malformations (3), but management of high-flow AVMs is often more problematic. AVMs grow commensurably with children or young adults, and patients develop significant symptoms

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None of the authors has identified a conflict of interest.

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and signs, such as pain, swelling, bleeding, ulceration, and disfiguration, which require treatment. Historically, surgery was the primary treatment for AVMs, but cure was rare (4,5,6). Recently, embolization with various embolic agents has been proven as an effective treatment (7,8). In embolization, permanent occlusion of the nidus should be the goal. Proximal occlusion of feeding arteries usually results in collateral development to the nonoccluded nidus. It is essential to deliver embolic agents properly into the nidus, although no single embolic agent has emerged as "perfect."

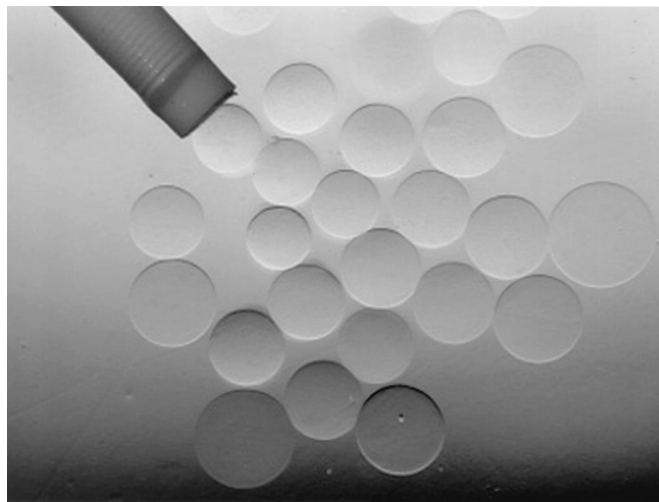
In Japan, no permanent embolic agent has been approved for peripheral vessel occlusion, including polyvinyl alcohol (PVA) particles and *n*-butyl cyanoacrylate (NBCA). Absolute ethanol can be an alternative agent for embolization of AVMs; however, it requires much caution and adequate experience to avoid serious ischemic damage to normal tissue (8).

Against the background of lack of availability of appropriate embolic agents for AVMs in Japan, the authors have developed an original particle embolic agent, a superabsorbent polymer microsphere (SAP-MS). Because the SAP-MS is spherical in shape and its particle size is calibrated, the occlusion level of embolized vessels can be estimated by choosing optimal particle size for individual abnormalities. Furthermore, the unique property of SAP-MS to expand by absorbing fluids after reaching the occlusion point may enhance the embolic effect of occluding vessels. The purpose of this report is to describe the authors' experience with use of SAP-MS in transarterial embolization (TAE) treatment of symptomatic AVMs and to determine its efficacy and safety and whether adjunctive embolization or surgery is required.

## MATERIALS AND METHODS

### Embolic Material

The SAP-MS (sodium acrylate and vinyl alcohol copolymer; Fig 1) is an embolic agent designed for use in the treatment of hypervascular tumors and AVMs. This material is a nontoxic and nonbiodegradable solid particle with a spherical shape. The particle



**Figure 1.** SAP-MS particles (size range, 250–300  $\mu\text{m}$ ) suspended in sodium meglumine ioxaglate 320 mgI/mL (Hexabrix320, Tanabe) are injected through a microcatheter (Rapidtransit, Cordis) with 0.021-inch inner diameter. The SAP-MS particle is deformable and can easily pass through the microcatheter. Note particles gradually expand by absorbing normal saline around the catheter within minutes.

size is calibrated in increments of approximately 50  $\mu\text{m}$  (range, 53–350  $\mu\text{m}$ ; ie, 53–106, 106–150, 150–212, 212–250, 250–300, 300–350  $\mu\text{m}$ ). The SAP-MS absorbs fluids and swells within several minutes. The diameter of a SAP-MS particle in an ionic contrast material, sodium meglumine ioxaglate 320 mgI/mL (Hexabrix320, Tanabe, Osaka, Japan), and human serum is approximately 2 and 3.5 times larger than its original size in dry state, respectively. When a SAP-MS particle suspended in sodium meglumine ioxaglate 320 mgI/mL (Hexabrix320, Tanabe) is transferred to human serum, it takes several minutes to swell again to the supposed size. After absorbing fluids, the swollen particle is soft and deformable, but maintains a spherical shape as it enlarges (9). The SAP-MS is usually suspended in sodium meglumine ioxaglate 320 mgI/mL (Hexabrix320, Tanabe) before injection and the suspension can be easily delivered via existing microcatheters without clumping. Because the SAP-MS takes several minutes to swell in the vessel after delivery, it reaches distally first to the vessel of comparable diameter with the particle size and swells at the occlusion point (9). The particle size of the SAP-MS described in this report is the size in dry state. A previous animal study reported long-term tight peripheral vessel occlusion with use of SAP-MS particles with limited perivascular reaction or inflammatory change in the surrounding tissue (9,10). As an

embolic agent, the SAP-MS was originally developed by Shinichi Hori, MD (9), and has not been approved by the Ministry of Health and Welfare of Japan or the Food and Drug Administration of the United States.

### Patients

Between July 1992 and September 2001, 27 patients with symptomatic congenital AVMs were referred for endovascular treatments. In this study, 25 of 27 patients (93%) who had symptomatic lesions and suitable vascular anatomy for transarterial approach ( $n = 23$ ) or underwent TAE treatment with primary use of SAP-MS particles for symptom palliation devascularization before surgery ( $n = 2$ ). The remaining two patients required primary sclerotherapy because their lesions were supplied by multiple small feeders and capillary or venous abnormality was dominant on baseline angiography. These two patients were excluded from this study. The 25 patients (16 men, nine women) included in this study had a mean age of 32 years with a range of 12 to 66 years. There were five patients with facial AVMs (one ear, one cheek, one cheek-lip, one orbit-cheek-lip, and one lip), eight patients with upper extremity and shoulder AVMs (UE-AVMs; two finger, one hand, one forearm, two forearm-hand, one arm-hand, and one shoulder-arm), and 12 patients with lower extremity and buttock AVMs (LE-AVMs; four foot, two knee, two thigh,

one thigh-knee, two buttock-thigh, and one buttock-knee). The diagnosis of AVM was based on clinical history, physical findings, and imaging studies, including ultrasound, computed tomography, magnetic resonance (MR) imaging, and angiography.

Onset of the symptoms varied from infant (< 3 y;  $n = 2$ ), childhood (< 10 y;  $n = 3$ ), teenage (< 20 y;  $n = 6$ ), to adulthood ( $\geq 20$  y;  $n = 14$ ). Pain and swelling were prominent symptoms in 17 and 24 patients, respectively. Seven patients (three UE- and four LE-AVMs) presented with skin ulceration. Seven patients (three facial, three UE-, and one LE-AVMs) experienced episodes of spontaneous bleeding. Other symptoms included weakness (two UE-AVMs), discoloration (one UE- and one LE-AVM). Four of eight UE-AVMs and four of twelve LE-AVMs involved a large area over more than one joint. Thirteen of 25 patients (52%) had undergone surgical interventions (ligation of feeders, partial resection, open biopsy, and below-the-knee amputation), and presented with recurrence or aggravation of their symptoms. Three patients (one UE- and two LE-AVM) had undergone TAE treatment with use of NBCA, absolute ethanol, or coils, and one patient with LE-AVM had undergone radiation therapy.

The authors elected on a patient-by-patient basis to use primarily SAP-MS particles and occasionally NBCA, both of which have not been approved by the Ministry of Health and Welfare of Japan. Special written consent forms were obtained from patients, which indicated that they understood that their condition was unique, there were no appropriate embolic agents approved for AVMs in Japan, and the use of these agents was preferred to control their symptoms and could be used safely. The internal review board was not available at the time this study began and the study followed the Declaration of Helsinki principles (11).

#### Embolization Technique and Follow-up

All procedures were performed with use of local anesthesia and no sedation or general anesthesia was used during the procedure in all patients. Baseline digital subtraction angiography (DSA) was performed in the same procedure as TAE in most

cases. Transfemoral approach was routine. Antegrade brachial and femoral approaches were alternatively performed in five patients with UE-AVMs, and six patients with LE-AVMs, respectively. A microcatheter with 0.013–0.024-inch inner diameter (Rapidtransit; Cordis, Miami, FL; Fast-Tracker 325; Boston Scientific/Mediatech, Natick, MA; Magic HO2/STD; Balt, Montmorency, France; On the Road; Soluton, Yokohama, Japan) was superselectively advanced coaxially through a 4–5 F guiding catheter (Selecon Catheter; Clinical Supply, Gifu, Japan; Glidecatheter; Terumo, Tokyo, Japan) as close as possible to the nidus. Selective DSA images were obtained to delineate the anatomy of the nidus and the timing of blood flow through the nidus. As the first choice of embolic agent, SAP-MS particles were primarily used for nidus occlusion. SAP-MS particles suspended in sodium meglumine ioxaglate 320 mgI/mL (Hexabrix320, Tanabe) with concentration of 10 mg/mL were injected through a microcatheter slowly and carefully with use of fluoroscopy to avoid reflux into normal branches. The sizes of the particles were estimated based on the size of the arteries entering the nidus. Smaller particles (size range, 53–150  $\mu\text{m}$ ) were preferred for the nidus with tiny vessels and slower filling of drainage veins, whereas middle particles (size range, 150–250  $\mu\text{m}$ ) to larger particles (size range, 250–350  $\mu\text{m}$ ) were preferred for microfistulous arteriovenous (AV) connections to prevent particles passing through AV shunting. Gelatin sponge particles (approximately 500–1000  $\mu\text{m}$ ) manually prepared from a gelatin sponge sheet (Spongel; Yamano-ouchi, Tokyo, Japan) were complementarily used to enhance the reduction of blood inflow to the nidus based on individual lesions. For macrofistulous AV connections with higher risk of migration of embolic agents toward the lungs, NBCA (Histoacryl; B-Braun, Melsungen, Germany) diluted with ethiodized oil (Lipiodol Ultrafluide; Guerbet, Villepinte, France) in 1:1–1:2 dilution was used; fibered coils were used as an alternative depending on the estimated diameters of AV fistulas on DSA images. These angiography or TAE techniques were combined with or without blood flow control with a tourniquet, blood pressure cuff, or 5-F

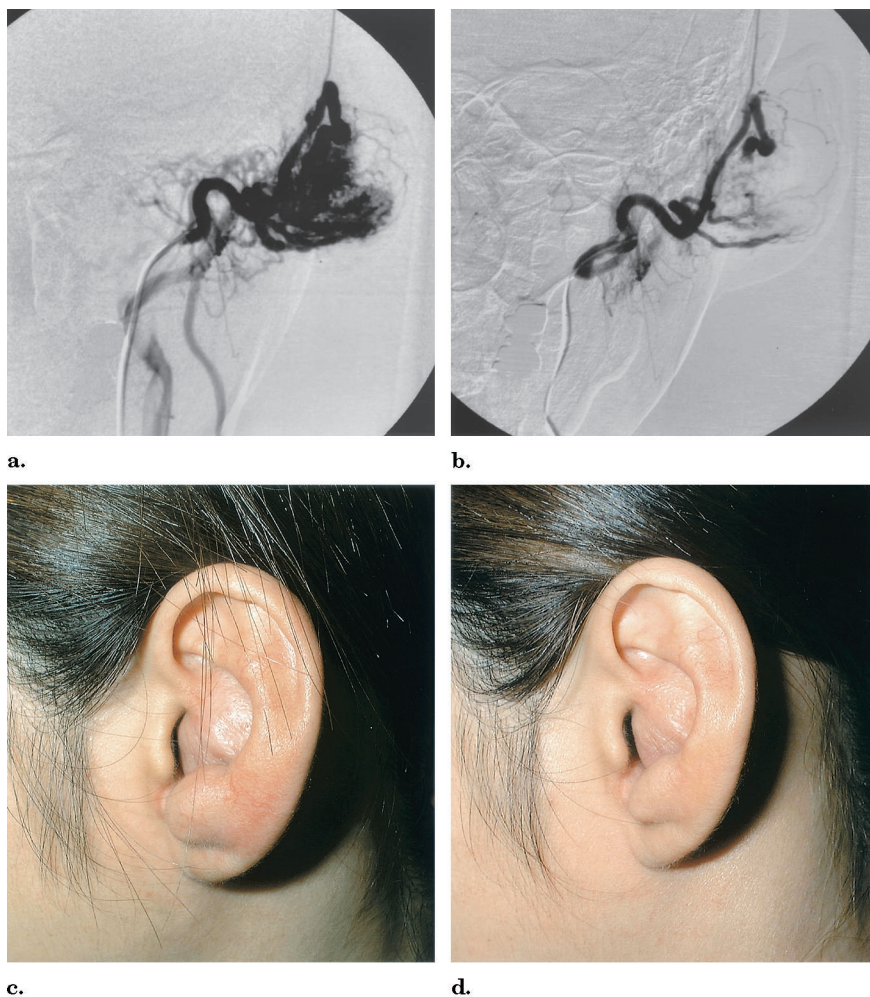
occlusion balloon catheter (Selecon Catheter; Clinical Supply, Gifu, Japan).

Direct puncture embolization (DPE) was employed in four cases mainly for occlusion of the tiny AV connections in slow-flow condition after arterial inflow reduction by TAE. As a sclerosing agent in DPE, the authors used 1% polidocanol (Aethoxysklerol; Kaigen, Osaka, Japan), which is detergent-type sclerosing agent commonly used in Japan for sclerotherapy of varicose veins of the lower extremities, or absolute ethanol. In embolization of hand and foot AVMs, the base of fingers and toes were bound by rubber bands to avoid non-target embolization of digital arteries.

The end point of embolization was determined based on significant reduction or cessation of the blood flow of the embolized artery on fluoroscopic observation or delay of venous drainage filling on control DSA. The authors preferred multistaged embolizations, especially when the lesion was large and complex, involving muscles and bones.

After the procedure, patients received intravenous fluids continuously and prophylactic antibiotics at 8 hour intervals until the next day. Oral nonsteroidal antiinflammatory agents were given according to local postprocedure pain. For multistaged embolization, treatment was repeated with 1–6-month intervals. As a rule, additional embolization was performed if the symptoms remained or recurred. In five patients, surgical interventions, including skin graft surgery ( $n = 1$ ; LE-AVM), excision ( $n = 1$ ; facial AVM), and amputation ( $n = 3$ ; UE-AVMs), were required when the patients presented with intractable ulceration or tissue necrosis. In two patients with facial AVM, surgical excision was considered to be necessary to reduce the bulk and improve the facial contour and the initial TAE procedure was performed preoperatively. Surgical specimens, including the nidus and the surrounding tissues, were obtained from four patients (one orbit-cheek-lip, one lip, and two finger AVMs) and examined histologically with use of hematoxylin and eosin and elastica-van Gieson staining.

Based on each clinical condition, follow-up was performed at intervals ranging from 3 months to 1 year.



**Figure 2.** A 31 year-old woman with left ear AVM who was referred because of frequent spontaneous bleeding. (a) The left posterior auricular arteriography (AP view) shows the diffuse nidus with early venous filling. (b) TAE was performed with use of SAP-MS particles (150–250  $\mu\text{m}$ ) alone. Postembolization DSA shows occlusion of the nidus. Proximal portions of the feeding arteries remain patent. (c) Photograph at the first clinic visit in August 2000 shows enlarged left ear with slight redness. (d) Photograph at 10-month follow-up after TAE treatment in September 2001 shows shrinkage of the ear without skin problems. No bleeding was experienced after TAE treatment.

Follow-up study included clinical findings and imaging studies, mainly Doppler ultrasound and MR imaging. A retrospective review of the available medical records was performed in September 2001. Clinical outcome was evaluated depending on the subjective improvement of symptoms and signs.

Complications were classified as major or minor according to the Society of Interventional Radiology reporting standards (12). Major complications result in an unplanned increase in the level of care, permanent adverse sequelae, or death. Minor complica-

tions result in no sequel with or without nominal therapy requirement.

## RESULTS

Seventy-two TAE procedures were performed in all patients (range, 1–11, mean, 2.8 per patient) and 12 DPE procedures were performed in four patients (range, 1–3, mean, 1.8 per patient). SAP-MS particles were used in 71 of 72 TAE procedures (99%). In only one TAE procedure in one patient with LE-AVM, SAP-MS particles were not used because of a large arterio-

venous fistula that was occluded with coils. SAP-MS particles were always easily delivered through a microcatheter and no catheter occlusion occurred because of clumping or expansion of the SAP-MS particles. SAP-MS particles with smaller (53–150  $\mu\text{m}$ ), middle (150–250  $\mu\text{m}$ ), and larger (250–350  $\mu\text{m}$ ) diameter range were used in six cases, 18 cases, and 16 cases, respectively. A small amount of gelatin sponge particles were complementarily added in 13 cases. For occlusion of fistulous AV connection, NBCA and coils were alternatively used in three and five cases, respectively. For DPE, absolute ethanol was used in one case with facial AVM, and 1% polidocanol was used in three cases (two UE- and one LE-AVMs). The mean length of follow-up was 38 months (range, 7–110 mo). Seven patients were lost to follow-up after the mean length of 45 months (range, 19–71 mo). In these patients, the clinical outcome was determined based on the medical records from the last date of an outpatient clinic visit.

In three of 25 patients (12%), the lesions were totally removed by surgical excision (one lip AVM) and amputation (two finger AVMs) after embolization without later recurrence of symptoms. In 20 of 25 patients (80%; four facial, five UE-, and 11 LE-AVMs), symptoms were improved by embolization alone ( $n = 17$ ) or in combination with surgical means ( $n = 3$ ). In these patients, the outcome was recognized as symptomatic palliation indicated by pain relief, shrinkage, ulcer healing, no bleeding, and improvement of weakness or discoloration. Two of 25 patients (8%; one arm-hand and one foot AVM) showed recurrence or no improvement of the symptoms and signs during follow-up.

## Facial AVMs

In facial AVMs ( $n = 5$ ), disfigurement because of swelling was the main problem. In addition, spontaneous bleeding was experienced in three patients. In one case of ear AVM and one case of cheek AVM, satisfactory shrinkage of the lesion was obtained by TAE alone, and they remained asymptomatic (Fig 2). In one case of cheek-lip AVM, the initial preoperative TAE was insufficient to control intraoperative bleeding and the ipsi-

lateral external carotid artery was ligated. As intermittent oral oozing persisted, an additional TAE procedure was performed via the surgically exposed ipsilateral superficial temporal artery, resulting in hemostasis, and the patient remained asymptomatic during follow-up. In one case of orbit-cheek-lip AVM, the main feeders from the external carotid artery were preoperatively embolized followed by partial excision after 3 days with minimal blood loss. The facial contour was improved without recurrence of symptoms. In one case of lip AVM, marked shrinkage was obtained after two TAE procedures. For further reduction, DPE was attempted with use of absolute ethanol; however, it resulted in mucosal necrosis requiring plastic surgery. The lesion was totally removed with a satisfactory cosmetic result and there was no later recurrence.

#### UE-AVMs

In UE-AVMs ( $n = 8$ ), pain ( $n = 5$ ) and swelling ( $n = 8$ ) were dominant symptoms. Intractable ulceration was seen in three cases and was accompanied by bleeding in two cases. In two cases with finger AVM, TAE treatment failed to improve the symptoms and both fingers were amputated. In one case of hand AVM, the lesion was prominent on the palm and severely painful. TAE treatment followed by DPE of the nidi with use of 1% polidocanol resulted in shrinkage of the lesion with pain relief. In three forearm cases, symptoms were improved by TAE alone. In one case of entire upper-extremity AVM, pain and ulcer in the hand were not controlled by embolization alone and severe skin necrosis was reported at two-year follow-up. The patient underwent amputation at the distal forearm with good stump healing, but pain and swelling recurred more proximally in the arm 1 year later. In one case of shoulder-arm AVM, swelling and weakness of the arm was improved by repeat TAE procedures.

#### LE-AVMs

In LE-AVMs ( $n = 12$ ), pain ( $n = 10$ ) and swelling ( $n = 11$ ) were dominant symptoms in addition to skin ulcer ( $n = 4$ ), bleeding ( $n = 1$ ), and discoloration ( $n = 1$ ). Pain relief was obtained

by embolotherapy alone in nine cases and all of these patients walked well without restriction. Ulcer was intractable in two cases. In one case of foot AVM, the infiltrative diffuse AV shunting was noted on DSA. The painful ulcer was not controlled by TAE treatment and the patient was lost at 21-month follow-up with unhealed skin ulcer. Another patient with thigh-knee AVM, who underwent amputation below the knee because of foot necrosis 12-years previously, developed skin ulcer with frequent, severe bleeding associated with leg prosthesis. With repeat TAE procedures and skin graft surgeries, the ulcer was slowly healed without further bleeding. The patient was confined to a wheelchair during most of the follow-up period, but recently started walking on prosthesis again (Fig 3). In a case of buttock-thigh AVM, TAE treatment resulted in shrinkage of the lesion with improvement of discoloration and ulceration.

#### Histological study

Histological specimens were obtained in patients with two facial AVMs, and two finger AVMs. SAP-MS particles penetrated into abnormal vessels of the target lesions, and occluded the vessel lumen tightly with each single particle. The particles deformed and conformed to the vessel lumen, stretching the vessel wall without disrupting it. Perivascular reaction was minimal and no angioneurosis was observed. Chronic foreign body reaction was shown in one patient with lip AVM, who underwent surgery three months after the first TAE procedure. No significant perivascular reaction was found in cases with finger AVM, although it was many months since their initial TAE procedure. No inflammatory reaction or ischemic tissue damage was observed in the surrounding tissue (Fig 4). These findings revealed the inertness of SAP-MS particles and the mechanism of embolic effect of SAP-MS particles mainly depended on mechanical properties rather than thrombogenic or fibrogenic properties.

#### Complication

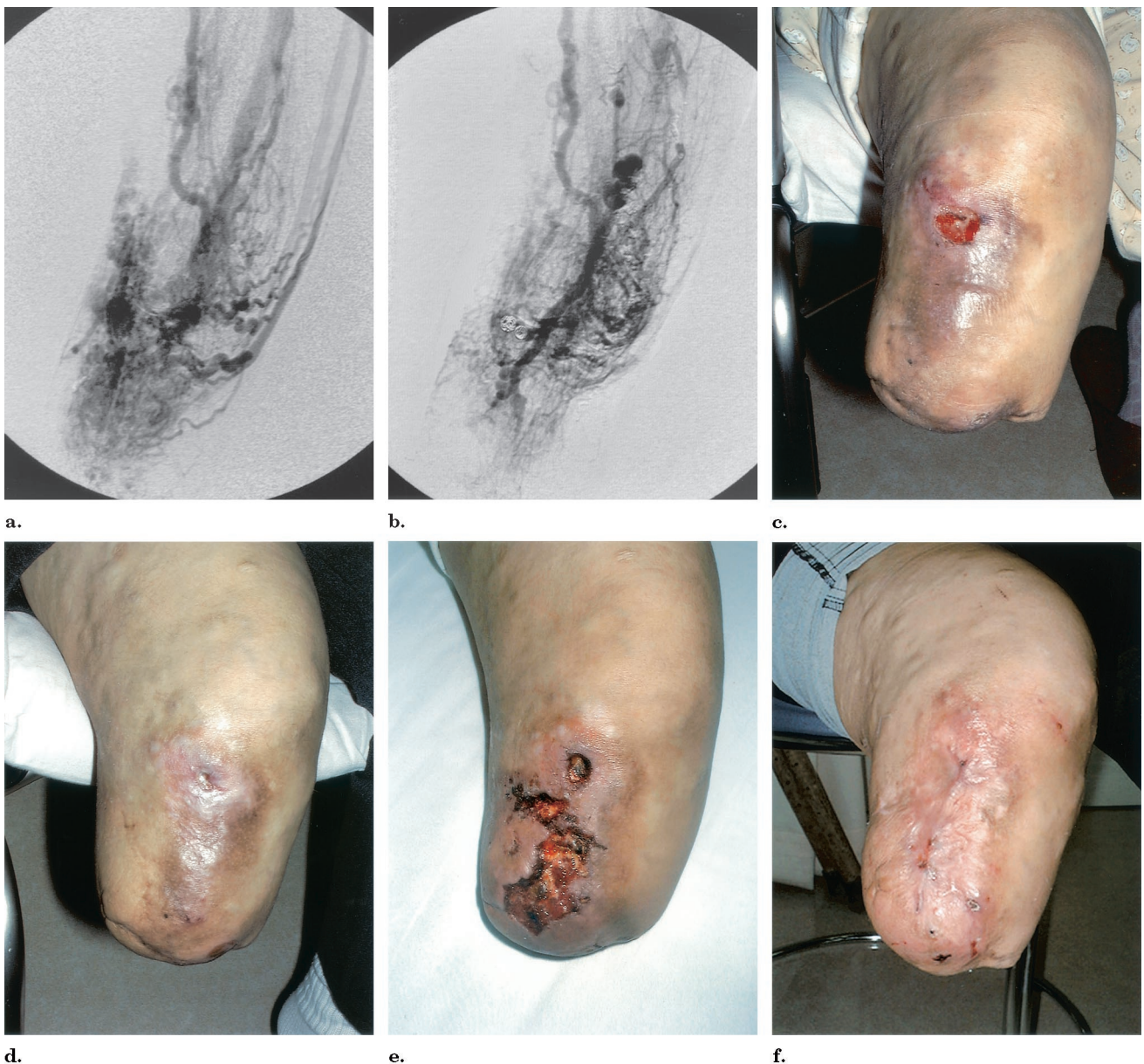
No major complications occurred after TAE treatment with use of

SAP-MS particles. Local swelling and pain were experienced in most cases for a few days and were well controlled with nonsteroidal antiinflammatory agents. No ischemic complication, such as tissue necrosis or nerve injury, was associated with TAE treatment with use of SAP-MS particles. In a case with lip AVM, the mucosal necrosis was induced by ethanol injection and was treated surgically.

#### DISCUSSION

Efficacy of transarterial or direct puncture embolization for AVMs has been reported with use of various embolic agents including PVA (13,14,15,16,17), NBCA (7,18,19), ethanol (8), and others (20,21). Although most of them were considered to be "effective" in short- to mid-term follow-up, there have been few reports describing long-term efficacy of each agent.

In the current study, the authors described their experience with use of SAP-MS particles in the management of facial and extremity AVMs with a mean follow-up period of 37.8 months. Although follow-up was not long enough to reach a conclusion, symptom palliation was achieved in 80% of cases by TAE treatment alone with primary use of SAP-MS particles or in combination with surgery. No ischemic complication, such as tissue necrosis and nerve injury, was observed after TAE treatment with use of SAP-MS particles. The histological study showed SAP-MS particles penetrating into intralumenal abnormal vessels corresponding with particle size with minimal perivascular reaction. No ischemic damage was observed in the surrounding tissues because SAP-MS particles did not reach the capillary level and spared microcirculation of normal tissues. These findings suggest that inert and precisely calibrated SAP-MS particles are preferable embolic agents in TAE treatment of facial and extremity AVMs, where normal tissues are often fed by the same embolized artery. In facial AVMs, neurological complications, such as cranial nerve injury, blindness, and cerebral stroke, may be avoided with use of calibrated SAP-MS particles with a diameter larger than the critical arteries supply-



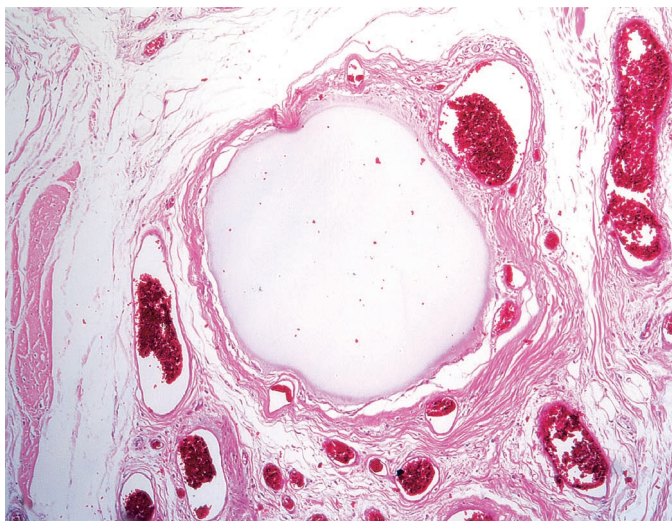
**Figure 3.** DSA images and photographs of a 21-year-old woman with extensive LE-AVM, who had undergone below-the-knee amputation at 8 years of age as a result of tissue necrosis. **(a)** In February 1999, the baseline right superficial femoral arteriography shows extensive AVM with multiple nidi around the knee. **(b)** At the third TAE procedure in May 1999, the postembolization image shows the reduction of AV shunting. SAP-MS particles (150–350  $\mu\text{m}$ ) were mainly used in addition to NBCA and coils. **(c)** At the first clinic visit in February 1999, the patient developed an ulcer with episodes of severe bleeding, which was associated with leg prosthesis. Varicose veins are noted on the lateral aspect of the thigh. The bruit was prominent around the knee. **(d)** In August 1999, after four TAE procedures, the ulcer was improved. Three more TAE procedures were performed for further reduction of the blood flow into the nidi without complication. **(e)** In August 2000, as the patient's activity increased, the ulcer was aggravated. Debridement and skin graft surgery were required. **(f)** In September 2001, the ulcer was almost healed with bruit remaining reduced.

ing cranial nerves or connecting to internal carotid circulations.

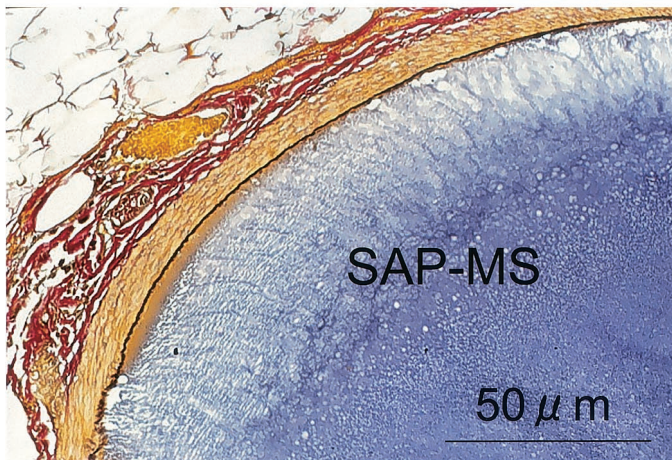
In large or complex lesions, the authors preferred multistaged embolizations to reduce the risks associated with a long procedure (8,22). In many extremity AVMs, pain was the pri-

mary indication for embolization, and most patients responded well to treatment. Considering the benign condition of the disease, the authors stressed the safety of the procedure and palliation of symptoms in their patients.

The goal of preoperative embolization is to achieve effective devascularization, minimize intraoperative blood loss, and facilitate subsequent surgical excision (17). Because it causes intraleisional vessel occlusion with minimal inflammatory changes in the sur-



a.



b.

**Figure 4.** (a) Finger AVM. The finger was amputated 2 years after TAE treatment with use of SAP-MS particles (53–106  $\mu\text{m}$ ). SAP-MS particles kept the vessel lumen completely occluded. Hematoxylin and eosin stain ( $\times 40$ ). (b) Facial AVM. The specimen of the cheek was obtained three days after TAE treatment with SAP-MS particles (250–300  $\mu\text{m}$ ). The internal elastic membrane is stretched because of the swollen particle. No perivascular reaction is seen. Elastica-van Gieson stain ( $\times 200$ ).

rounding normal tissue, TAE treatment with use of SAP-MS particles will result in effective preoperative embolization.

TAE treatment failed to improve the symptoms in two patients. Both of them had diffuse and infiltrative lesions with intractable ulcerations and pain. The outcome in these two patients is similar to that reported by Upton et al (3) and White et al (7). As described in their long-term follow-up reviews, diffuse UE-AVMs, involving all tissues of the arm (Upton type C), or diffuse LE-AVMs, involving all trifurcation arteries, are very difficult to treat and often require amputation.

DPE has been reported as another useful approach in AVMs (18,23,24). DPE was performed in certain cases, mainly to occlude the tiny AV connections in slow-flow condition after TAE

treatment, but the authors experienced one ischemic complication, which was associated with ethanol injection.

The choice of embolic agent was based on the individual abnormality and the desired therapeutic effect. Temporary agents are not effective and the use of permanent agents is essential to obtain long-term occlusion of AV shunting, especially when the embolization is a primary treatment. For preoperative embolization, inert agents that cause less inflammatory reactions are preferable. However, in Japan, there is no approved permanent embolic agent appropriate for the nidus occlusion. In this series, the authors occasionally combined SAP-MS particles with complementary use of gelatin sponge particles, which is an exclusively popular “temporary” agent in Japan, but they believe that

the embolic effect primarily depends on that of SAP-MS particles.

PVA is the most commonly used for many diseases worldwide. Despite its historic use in facial and extremity AVMs (13,14,15,16,17), several drawbacks of PVA have recently been recognized. The tendency of PVA particles to clump together often results in proximal feeder occlusion, which is not suitable for TAE treatment of AVMs. Recanalization also can occur, when organized thrombi in the space between clumps of PVA particles are reabsorbed (25,26).

Tissue adhesive, initially isobutyl-2 cyanoacrylate (14,23), now replaced by NBCA (7,18,19,27), has been used as the preferable agent for facial and extremity AVMs. An ideal NBCA/Lipiodol mixture polymerizes in the nidus and partial or total occlusion of the nidus can be achieved. However, mastering the technique of use of NBCA is difficult. An inappropriate NBCA/Lipiodol mixture may result in proximal feeder occlusion or passing through AV shunts and reaching the lungs. In addition to the difficulty in controlling the occlusion level, catheter gluing or occlusion is problematic (28,29,30). White et al (7,14,31) reported their current use of NBCA/Lipiodol mixture in a 1:2 or 1:3 dilution based on their laboratory and clinical works.

The Embosphere Microsphere (Biosphere Medical, Rockland, MA) particle, a precisely calibrated microsphere particle, is a new commercially available embolic agent in Europe and North America and has quite similar properties to SAP-MS particles. Beaujeux et al (32), the first use of Embosphere Microsphere (Biosphere Medical) particles to treat AVM, reported successful TAE treatment of facial, spinal cord, and cerebral AVMs. Similar to the authors' experience with use of SAP-MS particles, the precise control of occlusion level with use of a calibrated microsphere with an optimal diameter contributed to the safety for TAE treatment of craniofacial and spinal AVMs. At present, the use of Embosphere Microsphere (Biosphere Medical) particles in extremity AVMs has not been reported. The difference in the embolic effects between SAP-MS and Embosphere Microsphere (Biosphere Medical) particles is unknown.

Among the currently available

agents, absolute ethanol has demonstrated its curative potential with long-term improvement of symptoms in the treatment of vascular malformations, according to a large report by Yakes et al (8,22,24,33,34,35). Absolute ethanol has been rather commonly and effectively used for treatment of low-flow malformations (venous and lymphatic) (35,36,37), whereas its use for high-flow AVMs requires extreme caution and superselective catheter placement to avoid tissue necrosis and neuropathy. However, the complication rate was rather high, as much as 10% including temporary neurological episodes and skin injuries (8).

In conclusion, SAP-MS particles were used safely in embolization of AVMs based on their inertness and calibrated spherical feature. The clinical outcome of TAE treatment with use of SAP-MS particles was acceptable, but diffuse and infiltrative lesions remain challenging for embolotherapy as a primary treatment. Alternative methods or principles may need to be adopted in further treatment. Multidisciplinary management by interventional radiologists and other specialized physicians should be mandatory, with long-term follow-up of patients to evaluate the efficacy of the treatment.

**Acknowledgments:** The authors thank Robert I. White, Jr., MD, for his editorial assistance, and Saki Osuga, MD, Fumiaki Isohashi, MD, and Ms. Yukari Tanaka for their help in the preparation of this manuscript.

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