# Embolotherapy of Peripheral Arteriovenous Malformations

Advances in embolic agents and microcatheter techniques have allowed more successful treatment of this uncommon clinical entity.

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he understanding of the pathophysiology and treatment strategies of congenital vascular malformations has advanced significantly during the past decade. The classification system of vascular birthmark abnormality should be based on certain clinical applicability, and it is best divided into two main types: hemangiomas and vascular malformations.<sup>1,2</sup> Hemangiomas are benign vascular tumors with a predictable proliferative stage in pediatric patients between 2 weeks and 18 months of age. 1,2 Hemangiomas tend to be small or absent at birth. They have a predictable involutionary stage between 2 and 6 years of age. The majority of hemangiomas require no treatment because they are self-limiting processes. A few hemangiomas do require interventions because of their anatomic locations or their pathologic activity, such as platelet trapping leading to hemorrhage. The majority of these lesions need no specific treatment except reassurance to the parents.

In contrast, arteriovenous malformations (AVMs) are always present at birth and grow with the patient.<sup>1</sup> Although this may not be clinically apparent in a child, a vascular malformation does not involute. They represent congenitally abnormal connections between arteries and veins devoid of the usual arteriolar resistance vessels or capillary beds. Vascular malformation typically follows a normal growth pattern without malignant potential. They are frequently asymptomatic but can expand sporadically in puberty and are frequently exacerbated by pregnancy or after local trauma.

Vascular malformations can be further subdivided into the categories of low-flow or high-flow lesions, which have therapeutic implications. Low-flow malformations are far more common than high-flow malformations and include venous, lymphatic, or mixed malformations.<sup>3</sup> The treatment strategies for low-flow vascular malformations are compression garments, percutaneous sclerosis, and surgical excision.<sup>4</sup> In contrast, high-flow malformations are extremely rare and are far more difficult to treat. Surgical ligation of the feeding arteries of a high-flow AVM is ineffective at best and often results in rapid recruitment of collaterals, which may render subsequent interventions ineffective.<sup>5,6</sup> Recent advances in endovascular interventions have provided a less-invasive percutaneous therapeutic strategy in the management of these



Figure 1. A symptomatic pelvic/perineal AVM with multiple feeding arterial branches originated from hypogastric arteries and femoral arteries.

high-flow AVMs. Nonetheless, due in part to the rarity of this condition, available literature of percutaneous embolotherapy in patients with AVM remains limited.

#### PATHOPHYSIOLOGY OF AVM

AVMs can exhibit aggressive proliferative behaviors because the majority represent the residual remnants of a developmental arrest in the early stage of embryonic life. They have a tendency to undergo a more destructive potency. The dominant effect on the surrounding tissues is largely caused by the AVM lesion itself, with compression and erosion. Secondary effect may involve hemodynamic processes such as potential arterial steal phenomenon or heart failure due to high-flow arteriovenous shunting. Peripheral tissues can be influenced in a variety of symptoms ranging from distal ischemia to gangrene, venous stasis dermatitis, and ulcer or gangrene caused by venous hypertension.<sup>7-9</sup> Frequently, AVMs have a high

recurrence rate because of their origin from the mesenchymal cells at an early stage of embryogenesis.<sup>4</sup> They retain the evolutional tendency to grow, which is frequently represented as a recurrence from a clinical perspective.<sup>10</sup> As such, the behavior pattern of AVMs is unpredictable. AVMs frequently proliferate as a result of various stimulations such as injury or surgical intervention, or a systemic hormone effect caused by pregnancy. These types of local or systemic stimuli can trigger an explosive growth of AVMs. Inadequate treatment of AVMs can often stimulate dormant AVMs to undergo rapid proliferation, thus rendering the condition worse. Clinical trademarks of AVMs are rapid recurrence and unbridled growth after incomplete treatment.

The concept of a vascular nidus is critically important in understanding these vascular abnormalities. The nidus is the central confluence of the malformation where the shunting of arterial blood to a vein occurs. The nidus can be large and spread out or may be multiple. Obliteration of the nidus will permanently cure an AVM. Unfortunately, this is not always possible when an AVM contains multiple or a large nidus(es). AVMs cannot be cured by proximally blocking the arteries by embolization, surgery, or other means that supply the nidus. The stimulation to form collaterals is always available and extremely powerful. In fact, incomplete embolization or surgical ligation of



Figure 2. A painful peripheral AVM located at the right foot causing recurrent bleeding and ulceration secondary to venous hypertension.

the supplying arteries makes the subsequent interventions more difficult, or sometimes even impossible.

#### **CLINICAL SYMPTOMS**

The clinical behaviors of AVMs vary greatly and can remain dormant for years before exhibiting symptoms. Many AVMs are clinically silent or present minimal clinical or cosmetic symptoms, whereas others are associated with debilitating conditions, such as varicosities and venous stasis ulcers due to venous hypertension, pain and pressure from mass effect, or potential hemorrhagic and ischemic complications. Occasionally, large AVMs may lead to congestive heart failure as the result of increased cardiac output.

Although AVMs can occur anywhere in the body, the pelvis and the extremities are the most common locations for peripheral AVMs. Pelvic AVMs may produce severe pain, pelvic congestion, sexual dysfunction, and occasionally, high-output cardiac fail-

ure and hemorrhage. Although the primary blood supply of pelvic AVMs is from hypogastric arteries, there may be multiple feeding branches from the inferior mesenteric artery, middle sacral artery, lumbar artery, and femoral arteries (Figure 1). Because of the complexity of feeding branches, complete surgical treatment is often not possible, and recurrences after successful surgical intervention are common.<sup>5,11,12</sup> Extremity AVMs may be associated with varicosities and superficial phlebitis. Occasionally, ischemic ulcerations or areas of tissue breakdown with bleeding are present due to both venous hypertension and arterial ischemia, which are caused by preferential flow to the AVMs at the expense of normal tissue (Figure 2). Extremity lesions in children may lead to leg length discrepancy, as well as disfiguring bone and soft tissue overgrowth if left untreated.<sup>1,6</sup>

#### TREATMENT INDICATIONS

Despite extensive efforts made to improve the outcome of managing AVMs, they remain one of the most challenging diagnostic and therapeutic dilemmas in vascular and endovascular surgery. Due to significant risks of surgically related complications and lack of malignant potential of AVMs, asymptomatic and mild symptomatic lesions typically do not require treatment. Commonly utilized clinical criteria of treatment indications for AVM,

# TABLE 1. TREATMENT INDICATIONS FOR AVM

#### **Absolute Indications**

- · Hemorrhage, major or recurrent minor
- Gangrene or ulcer of arterial, venous or combined origin
- Ischemic complication of acute and/or chronic arterial insufficiency
- Progressive venous complication of chronic venous insufficiency with venous hypertension
- High-output cardiac failure—clinical and/or laboratory
- Lesions located at life-threatening vital areas that compromise seeing, hearing, eating, or breathing

#### Relative Indications

- Various symptoms and signs affecting the quality of life; disabling pain and/or functional impairment
- Lesions with a potentially high risk of complications (eg, hemarthrosis) and/or limb-threatening location
- Vascular-bone syndrome with limb length discrepancy
- Cosmetically severe deformity with/without functional disability

which are listed in Table 1, are categorized to either absolute or relative indications. Among the absolute treatment indications, commonly encountered clinical scenarios that warrant interventions include hemorrhage, secondary ischemia due to proximal steal, and high-out-put congestive heart failure as a result of arteriovenous shunting. Examples of commonly encountered relative indications include disabling pain and pressure due to the mass effect, AVM-induced functional impairment, and cosmetic deformity such as limb asymmetry.

#### TREATMENT STRATEGIES

Complete elimination of the nidus of an AVM is the only possibility for a total cure. However, this is often difficult to accomplish. Symptomatic AVMs are traditionally treated by surgical resection or ligation. However, surgical resection is challenging partially due to multiple associated feeding arterial branches and the frequent inaccessible locations of an AVM, while ligation of the feeding arteries does not provide long-lasting results because recruitment of surrounding feeding collaterals are common. Historically, many surgical attempts made to control these ever-challenging problems have been inadequate or even disastrous, partly due to a poor understanding of the complicated nature of the conditions and sometimes due to ill-planned surgical approaches. Debulking, incomplete resection, or ligation of arterial branches leads to recurrence of the malformation.<sup>4,12</sup> Proximal ligation of feeding

vessels has been particularly catastrophic, resulting in continued enlargement of the fistula and increased recruitment of numerous smaller feeding and draining vessels, whereas an overly aggressive approach often leads to disfiguration, and even major amputation.<sup>13</sup> Additionally, difficult surgical exposure and extensive blood loss are common during surgical resection of deep AVMs.

The disappointing results of surgical treatment, related to its propensity for complications and recurrence despite successful operation, have kindled interests in evaluating other alternative approaches. Embolotherapy, since its original clinical inception in the early 1970s, has emerged into an extremely useful clinical tool for controlling hemorrhage and palliation of malignancies. 14,15 With technical advancements in microcatheter systems and embolic agents, embolotherapy has evolved into a valid alternative to surgery in treating AVM. This catheter-based endovascular intervention, used either in conjunction with surgical resection or used alone, provides a potentially safe alternative in treating AVM. It is a less-invasive treatment strategy to intentionally induce vascular thrombosis. This treatment strategy has been widely used to control active bleeding, such as gastrointestinal bleeding, pelvic trauma, and varices. Embolotherapy, although relatively safe, should be undertaken only for compelling indications. The goal of the treatment is to occlude the nidus of the primitive vessels through superselective catheterization of feeding branches. Multiple embolic agents can be used, including coils and detachable balloons, foam pledgets, particles, and liquid agents.

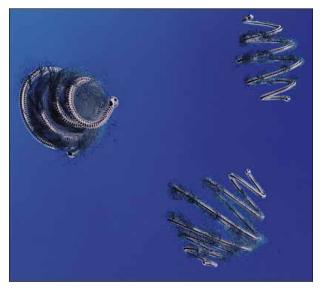


Figure 3. The coil (VORTX coil, Boston Scientific Corporation, Natick, MA) is constructed from a preshaped guidewire with attached wool or Dacron fibers that are dispersed along the length of the wire to enhance thrombogenicity.

#### **EMBOLIC AGENTS**

#### Coils and Detachable Balloons

Coils, either platinum or stainless steel, have been a mainstay of embolotherapy for the occlusion of large vessels. The coils are constructed from a preshaped guidewire with attached wool or Dacron fibers that are dispersed along the length of the wire to enhance thrombogenicity (Figure 3). Various sizes of coils are available and many can be introduced through a standard selective catheter by standard guidewire. One must pay attention to manufacturer's instructions to ensure the compatibility of the coils and catheter. For example, stainless steel coils should not be deployed through catheters made of polyurethane because coils may be trapped in the distal tip of the catheter, whereas polyethylene and braided nylon catheters are suitable for the deployment. Often, testing the coil-catheter-guidewire introducer may be necessary prior to its use on the patient.

Selecting the correct coil size is extremely important for the success of the procedure. The coils should be slightly oversized relative to the diameter of the target vessel to allow them to grip the vessel wall and be closely packed. Significantly oversized coils tend to pass through the vessel like a guidewire and may protrude to a feeding branch rather than coiling up. Undersized coils may fail to lodge and migrate causing unintended embolization by reflux into other vessels. Specialized coils have detachment mechanisms. Once the coils are placed in the appropriate location, an electric current is applied to allow the coils to detach from the insertion device.

Detachable balloons are used to occlude large arteriovenous communications, such as pulmonary AVMs, where coil occlusion may be hazardous. The advantage of detachable balloons is that a partially inflated balloon may be directed and lodged into the AVM by the natural direction of the blood flow. Additionally, the position of the balloon and the adequacy of the occlusion can be checked before balloon detachment.

#### Foam Pledgets

Foam pledgets are used for temporary occlusions that last several weeks. Gelfoam (Pfizer, Inc., New York, NY), one of the most commonly used, is fairly thrombogenic, and typically lasts 1 to 2 weeks before vessel recanalization. The Gelfoam is cut into small pieces and soaked in the diluted contrast medium to increase radiopacity prior to being loaded into the catheter. Once the catheter is in the desired location, a forceful injection or passage of a guidewire is often adequate to clear the catheter lumen and direct the Gelfoam to the nidus. Reflux and embolization of Gelfoam to inappropriate branches may be potential problems if the catheter tip is not sufficiently advanced into the desired vessel or if the flow is stagnant.

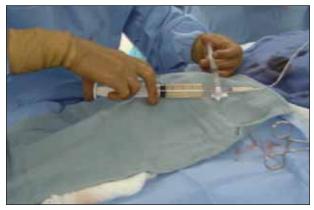


Figure 4. The mixture of PVA particles and diluted contrast material is being agitated vigorously before delivery to prevent particle clumping.

#### **Particles**

Polyvinyl alcohol (PVA) particles are the most commonly used particles that are available commercially in preselected sizes, ranging from <100 μm to >1,000 μm. PVA particles are the embolic agents of choice for the majority of embolization treatments. The particles wedge in the vessels of corresponding diameter and produce a permanent occlusion by thrombosis and fibrosis. The PVA particles tend to aggregate into larger particles in the delivery syringe prior to delivery. Therefore, to prevent particle clumping, it is essential to vigorously agitate the mixture of PVA particles and contrast just prior to delivery (Figure 4). The particle-contrast suspension is injected slowly in small aliquots under continuous fluoroscopic control once the delivery catheter is parked in the desired location. To decrease risk of reflux and nontarget embolization, excessive force should not be applied during injection.

# Liquid Agents

Liquid occlusive agents, including sclerosants and glue, provide another alternative for vessel occlusion. The most commonly used sclerosant is ethanol, which causes vessel thrombosis by denaturing the endothelial cells. As ethanol passes through the vasculature, the flow in the target vessels slows down and the potential for reflux into nontargeted vessels increases. Therefore, it is typically injected through an occlusive balloon catheter to prevent reflux into nontargeted vascular beds. Once ethanol reaches a high-flow venous system, it is rapidly diluted. Nonetheless, ethanol, like other liquid embolic agents, is very difficult to control and is the least forgiving. Thus, it is not widely used in the treatment of AVM, and its utilization should be restricted to experienced interventionists.

Glue or tissue adhesive, such as N-butyl cyanoacrylate (NBCA) and isobutyl-cyanoacrylate, is another category of liquid embolic agents that polymerizes and hardens on contact with an ionic environment such as blood. To decrease reflux and minimize the errant passage of glue into the venous system, the flow velocity of an arteriovenous shunt may be reduced with other agents prior to the infusion of glue. The main advantage of tissue adhesive is the ability to rapidly reach an AVM. which enables it to occlude the nidus of an AVM more rapidly than other embolic agents. However, during the procedure, the catheter must be rapidly withdrawn after each injection to prevent catheter trapping, resulting in frequent, time-consuming catheter exchanges. Failure to withdraw the catheter rapidly augments the risk of gluing the catheter in place. Despite its cumbersome application process, this group of agents may be ideal for AVM embolization and has been approved by the FDA for cerebral AVM embolotherapy.

With marked increase in demand for interventional procedures, extensive research efforts have been made to develop newer, safer, and more permanent embolic agents and devices. Nonadhesive flexible polymers cur-

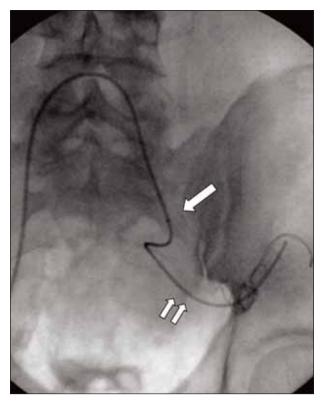


Figure 5. A selective catheter (double arrow) being advanced through the guiding sheath (single arrow depicting the tip of the guiding sheath) that is located at left hypogastric artery to secure the access of the desired artery.

rently under investigation may offer all the advantages of NBCA without its cumbersome application process. However, they are not yet approved by the FDA for use in human subjects.

# **DELIVERY SYSTEMS**

# **High-Quality Angiography**

The goal of embolotherapy AVM is to occlude the nidus and minimize nontarget embolization. A thorough knowledge of the vascular anatomy is a fundamental step to success before embarking on a procedure. A high-quality angiography to define the feeding arteries of AVM is crucial for preoperative planning. The interventionist should also be familiar with the collateral pathways; the shortest and straightest routes should be utilized for embolotherapy.

## **Guiding Sheath**

A guiding sheath is frequently used to secure the access and provide stability during a catheter exchange because the catheter may be occluded by the embolic agents. It allows for the replacement of the catheter without losing access (Figure 5). A guiding sheath is typically tracked over a .035-inch guidewire and secured at the orifice of the feeding branches, such as a branch of hypogastric artery for a pelvic AVM, and a branch of profunda femoral artery for a thigh AVM.

#### **Selective Catheter**

A variety of catheters are used to deliver embolic agents. The delivery catheter should be an end-hole catheter, which does not contain side holes. Side holes may cause the embolic agents to be trapped and lodged, leading to subsequent nontarget embolization. Additionally, a catheter with both an end hole and side holes has decreased expulsion force through the end hole, and therefore, increases the tendency of embolic particles to jam at the side holes. An occlusion balloon catheter may also be used to decrease the risk of reflux and nontarget embolization, particularly when liquid agents are used.

#### **Coaxial Catheter System**

Successful embolization of the nidus of an AVM often requires super-selective catheterization of numerous arterial feeding branches. This is facilitated by using coaxial microcatheter systems. A 2-F to 3-F microcatheter is coaxially introduced through a 4-F to 5-F selective catheter and can be manipulated into the terminal feeding artery (Figure 6). Embolic agents are then delivered via the microcatheter, which is ideal for delivering liquid agents, particles, and small coils.

### **RESULTS FOR CLINICAL SERIES**

Embolotherapy, along with high-quality imaging tools, has revolutionized the treatment of AVM. Development of coaxial microcatheter systems and various embolic agents further make embolotherapy a feasible and durable alternative to surgical therapy. There are increased numbers of therapeutic interventions utilizing embolization for peripheral AVM in recent years. Jacobowitz et al treated 35 patients with symptomatic pelvic AVM and reported an 83% symptomatic improvement during a mean follow-up of 84 months. 11 They also reviewed an additional eight series of a total 28 patients who were treated for pelvic AVM using transcatheter embolization techniques and demonstrated an 89% symptomatic improvement during a mean period of 29 months.<sup>11</sup> Jacobowitz et al recommended embolotherapy as the primary treatment modality for pelvic AVM while reserving surgical resection for patients with symptoms unimproved by embolization. Even so, embolization should be utilized as an adjunctive to facilitate surgical procedures.

In a study published in 1999, Upton et al reported their 28-year experience in the treatment of 270 patients with upper-limb vascular malformations, of which 33 were high-flow malformations. Although the majority of patients were treated by surgical excision, embolotherapy was used only in the last 5 years of their series. Although surgical excision was successful in localized lesions, patients with diffuse AVMs involving all tissues had ominous outcomes, with nine of 10 requiring amputation despite repeated excision and reconstruction. The authors also reported a 28% postoperative complication rate in all patients with high-flow AVMs who required treatment.

White et al reviewed their experiences of treating high-flow extremity AVM on 20 patients using tissue adhesive embolic agents.<sup>17</sup> They used isobutyl cyanoacrylate in the first nine patients and the remainder received NBCA. Follow-up was completed in eight of nine patients with lower-limb malformations (mean, 8.6 years) and in nine of 11 patients with upper-limb malformations (mean, 7.4 years). All patients with upper-limb lesions had significant symptomatic improvement, seven after embolotherapy alone and the other four after resection of high-flow AVM. In contrast, those with lower-limb high-flow AVM did poorly, with five of nine patients requiring amputation 1 to 6 years after technically and clinically successful embolotherapy. White et al concluded that embolotherapy alone or in combination with surgical resection provided excellent long-term palliation in patients with upper-extremity AVM, whereas lower-extremity AVM with diffuse involvement of all



Figure 6. A microcatheter (Renegade Hi-Flow microcatheter, Boston Scientific) that can be introduced through a selective catheter coaxially and manipulated to the terminal feeding artery.

three trifurcation arteries had higher rates of recurrence and amputation during an average of 8 years of follow-up.<sup>17</sup>

Another recent report by Sofocleous et al described a 15-year experience of NBCA embolotherapy involving 21 patients with upper-limb high-flow malformations.<sup>18</sup> Among them, 17 patients were diagnosed with highflow AVMs. Although the investigators noted an immediate technical success rate of 85%, which was defined as a more than 75% reduction or complete disappearance of the nidus, the clinical result was not long-lasting, with a mean symptom-free interval of 30 months. Moreover, among the eight treated patients with more than 2 years of follow-up, only two remained asymptomatic, whereas one underwent amputation, two had continuing pain, and three had persistent symptoms, including pain and swelling. The investigators noted that an average of 1.5 embolization procedures were performed per patient, and no major complications were documented. 18

Tan et al reported their experience of embolotherapy in 13 patients with high-flow extremity AVMs utilizing particles, glues, or a combination of both.<sup>19</sup> Tan et al recognized the challenging problem and recommended embolotherapy only for patients with significant symptoms. The investigators also concluded that multiple

treatment sessions were often necessary to eradicate the nidus. Last, Rockman et al recently reported their experience of 50 patients with extremity AVMs who were treated with embolotherapy, and they drew similar conclusions.<sup>20</sup>

# COMPLICATIONS ASSOCIATED WITH EMBOLOTHERAPY

Embolotherapy, although less invasive and relatively safe, is not without complications. Therefore, patients need to be fully informed of the potential risks of the treatment. The most common complications are infection and bleeding. Other potential complications include ischemia due to distal migration of the embolic agents and undesired embolization to branch vessels. Additionally, contrast-induced renal failure and anaphylactic shock may also occur.

Postembolization syndrome caused by tissue necrosis may be encountered after a successful embolotherapy. The symptoms of pain, fever, leukocytosis, and nausea arise shortly after embolotherapy and usually resolve within a few days; however, they may persist up to 1 week. Only close clinical observation and laboratory work-ups can distinguish postembolization from an infective complication. Compared to tumor embolization and organ embolotherapy, postembolization syndrome occurs less frequently after the treatment of AVM.

#### CONCLUSION

Peripheral AVM is a relatively uncommon clinical entity that presents a challenging dilemma to vascular surgeons today. With advancements in embolic agents and microcatheter techniques, embolotherapy has evolved into the mainstay of treatment for symptomatic and complicated peripheral AVMs. It provides reasonable safety and lasting therapeutic results with minimal risk of lesion recurrence. Nevertheless, a multidisciplinary approach and combination of surgical and embolization techniques are often necessary. As vascular surgeons, we need to have a thorough understanding of the anatomy, meticulous surgical skills, and proficiency in microcatheter techniques to effectively manage this ever-challenging clinical entity.

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