Interventional Treatment Options for Vascular Malformations

Approaches, techniques, and sclerosing and embolic agents that can be used in low- and high-flow vascular malformations.

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Vascular malformations comprise a group of lesions characterized by the presence of normal mature endothelial lining.[1,2] These lesions are usually present at birth, although not always noticed, and grow commensurate with the child's development. Jackson et al differentiated vascular malformations according to their flow features (ie, low- and high-flow lesions).[3] Low-flow vascular malformations include lymphatic, venous, and capillary malformations. The high-flow lesions are arteriovenous malformations (AVMs)/fistulas.[2,4]

Apart from capillary malformations, which are not usually treated with interventional therapy, all other types of vascular malformations can be treated with interventional techniques that typically require transarterial, transvenous, or direct access.[5] Interventional treatment of vascular malformations has gained wider acceptance in recent years and is considered the first line of therapy in many centers. The results of interventional treatment vary depending on the type of vascular malformation being treated.[2,4-20]

In this article, we discuss some of the techniques, agents, and approaches used in the interventional treatment of this difficult group of lesions. The reader should be aware and acknowledge that there are several different techniques and agents that can be used to treat these lesions. The techniques and agents described in this article have been used for years by the authors with good results.

LOW-FLOW VASCULAR MALFORMATIONS

Before discussing the interventional treatment of venous and lymphatic malformations, it is important to mention that because no arterial inflow is present, the use of catheter angiography for both diagnosis and treatment is unnecessary; therefore, the treatment of these lesions is performed through direct puncture for injection of the sclerosing or embolic agent most of the time. The diagnosis of these lesions can be made with a complete clinical history and exam and confirmed with Doppler ultrasound or magnetic resonance imaging (MRI). In our opinion, MRI with contrast is the method of choice because of its incomparable soft tissue visualization, which is used to determine the location, extension, and relationship with surrounding important structures, such as nerves, orbits, and airways. MRI often unveils lesions that are much larger than the clinical exam suggests. The use of MRI is particularly important in planning the treatment of craniofacial and head and neck lesions due to the aforementioned reasons.[16]

The technique that we use to treat low-flow vascular malformations differs slightly when treating venous and

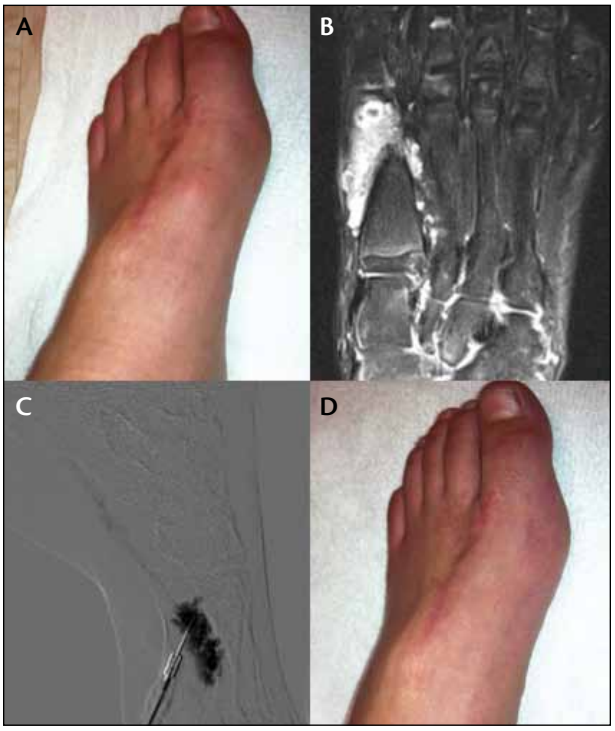

Figure 1. A 12-year-old boy with a history of resection of a left foot venous malformation 5 years ago presented with complaints of severe left foot pain. Clinical examination revealed a compressible bulging structure at the level of the first metatarsal artery (A). MRI T2 weighted images showed recurrence of the venous malformation (B). Venogram that was obtained after the lesion was accessed with direct puncture under ultrasound guidance (C). The lesion was successfully treated with STS. One month after the procedure, the left foot pain had completely resolved, and the initially visualized bulge was no longer seen (D).

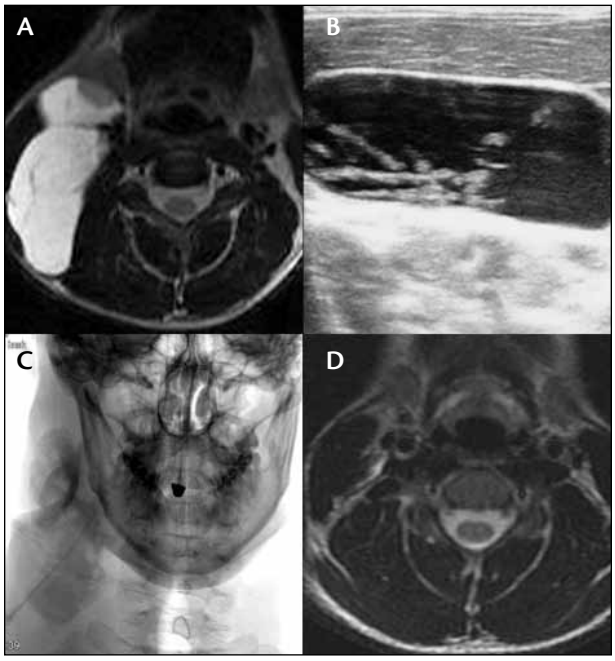

Figure 2. A 21-year-old man presented with a right neck mass. MRI (A) and ultrasound (B) revealed a large macrocystic lymphatic malformation. The lesion was percutaneously punctured under ultrasound guidance, and a 4-F catheter was placed. The lesion was treated with doxycycline (injection of opacified doxycycline) (C). A follow-up MRI 4 months after sclerotherapy demonstrated complete resolution of the lesion (D).

lymphatic malformations, and they will be explained separately. Some indications for treatment include pain, disfigurement, cosmetic improvement, limb length discrepancy and muscle atrophy, impingement on other organs, and heart failure. Not all lesions need to be treated, especially in asymptomatic patients, and expectations for outcomes need to be well managed because, in some cases, a complete cure may not be possible.

Our usual practice is to perform treatment under general anesthesia or moderate conscious sedation. The procedure takes place in an angiography suite with ultrasound guidance capabilities. The lesion is then accessed with direct puncture under ultrasound guidance. We usually use 21- to 25-gauge butterfly needles. For lesions that are too deep for the short butterfly needles, longer needles (eg, spinal needles) can be used. For large extensive lesions, multiple needles should be placed in different venous compartments. After slow venous return is seen through the needle, venography is performed to confirm correct placement of the needle, extravasation into surrounding soft tissues, and, most importantly, drainage into the adjacent venous system. Direct pressure or use of a tourniquet to control the outflow can be used. If fast drainage is seen into important regional veins that cannot be protected with direct pressure, sclerotherapy should be performed very carefully, and in such cases, a transvenous occlusion balloon can be placed and used to decrease flow. After determining the contrast volume necessary to fill the abnormal venous compartment, the same volume of sclerosing agent is infused slowly. In cases when there is concern regarding drainage of the lesion, the infusion is performed using the negative subtraction technique.[21] Lesions located in the orbit or airway are challenging because marked swelling from sclerotherapy may cause compartment syndrome or compromise the airway. In these cases, a sclerosing agent that causes less swelling, such as bleomycin, is preferred. Another option for these cases is preoperative embolization using liquid embolic agents such as Trufill

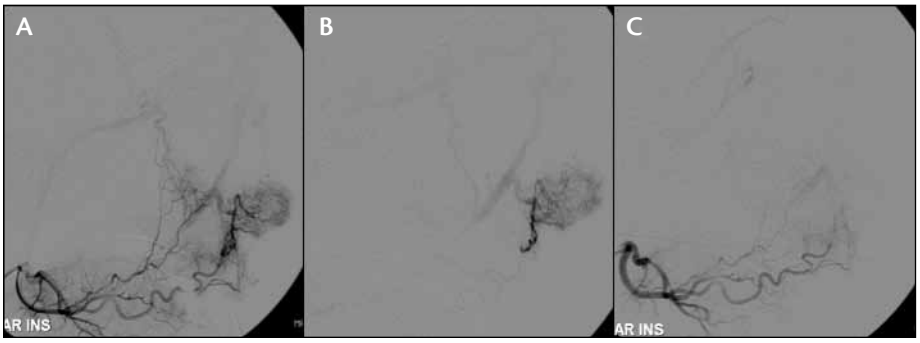

Figure 3. A 4-year-old girl presented with a history of epistaxis and known nasal AVM (A). A microcatheter injection demonstrated opacification of the nidus (B), which was then embolized using n-BCA diluted at 20% with near complete occlusion of the nidus (C). The patient has done very well, and 2 years posttreatment continues to be asymptomatic.

n-BCA (Codman Neurovascular, Raynham, MA) or Onyx (Covidien, Mansfield, MA). These embolic agents cause minimal or mild swelling and facilitate complete surgical excision of a localized lesion.[22]

Several agents have been used to treat venous malformations. The most commonly used agents in the United States are ethanol, bleomycin, and sodium tetradecyl sulfate (STS). Ethanol has been widely used, with maximum doses ranging from 0.5 to 1 mL/kg. It is highly effective; however, it also has higher rates of complications, which are mostly minor and transient. Lee et al studied 87 patients treated with ethanol sclerotherapy; 95% showed improvement, and complications were seen in 28% of the patients. Eleven patients had serious complications (ie, nerve injury, deep vein thrombosis, and muscle fibrosis).[23]

Similar results were seen by Berenguer et al. This series of 40 patients who were treated for craniofacial venous malformations showed a 75% cure/improvement rate. Complications included skin blistering (50%), deep ulceration (13%), and nerve injury (10%).[11] Other uncommon but dreaded complications of this therapy include pulmonary hypertension, cardiopulmonary arrest, seizures, rhabdomyolysis, hypoglycemia, and intoxication.[11,23,24]

STS has also been extensively used with good results (Figure 1).[19,25,26] We prefer to use it in its foam form to increase the surface of exposure, optimizing the sclerosing effect. To create the foam, we mix a syringe containing 5 mL of STS 3% and 1 mL of ethiodol with another syringe containing 5 mL of air through a three-way stopcock.[4] A good result or improvement is usually seen in 70% to 87% of cases, with an approximate 10% rate of minor transient complications and almost no major complications.

In a similar way, bleomycin has been shown to provide good results and an excellent safety profile.[5,17,18] Bleomycin is used at a maximum dose of 1 unit/kg or 15 units per session (concentration, 1 unit/mL). Sainsbury et al observed that in 42 patients with venous malformations who were treated with bleomycin, 30 were completely cured and eight showed significant improvement. There were no significant complications, but one lesion recurred.[5]

Another study analyzed 32 craniofacial venous malformations that were treated with bleomycin. The study looked at the pre- and postprocedure MRIs, as well as subjective improvement criteria (noted by clinicians and patients). Twenty-one lesions had decreased in size on the follow-up MRI (11 > 50% and 10 < 50% size reduction). Eleven lesions had no change. Minor transient complications were seen in 12.5%. Interestingly, despite the fact that 11 lesions had no change in size, subjective improvement was noted by clinicians and patients in 30 of 31 patients.[17]

Another study that compared ethanol to bleomycin in the treatment of facial venous malformations showed that ethanol had a slightly higher success rate and required fewer treatment sessions. On the other hand, bleomycin had a lower complication rate and less postprocedural swelling.[18] Other agents such as sodium morrhuate and polidocanol have been used with good results.[15,27]

LYMPHATIC MALFORMATIONS

Lymphatic malformations are the result of erratic development of lymphatic channels and are prone to infection, hemorrhage, pain, and mass effect.[4,12] They are divided into macrocystic, microcystic, and combined lesions. Interventional treatment is performed through direct puncture of the lesion under ultrasound guidance using a 21-gauge needle (Figure 2). It is our practice to place a small 4-F catheter in the macrocystic lesion. After the catheter is in a good position (as confirmed by ultrasound), the lymphatic malformation is completely aspirated. The sclerosing agent is then administered slowly through the catheter (approximately 80% to 90% of the aspirated volume). The catheter is left in place, and the sclerosing agent is allowed to dwell for 2 to 6 hours. The patient is then brought back to the procedure room, and aspiration is attempted to check for fluid re-accumulation. Depending on the size of the lesion, the catheter is

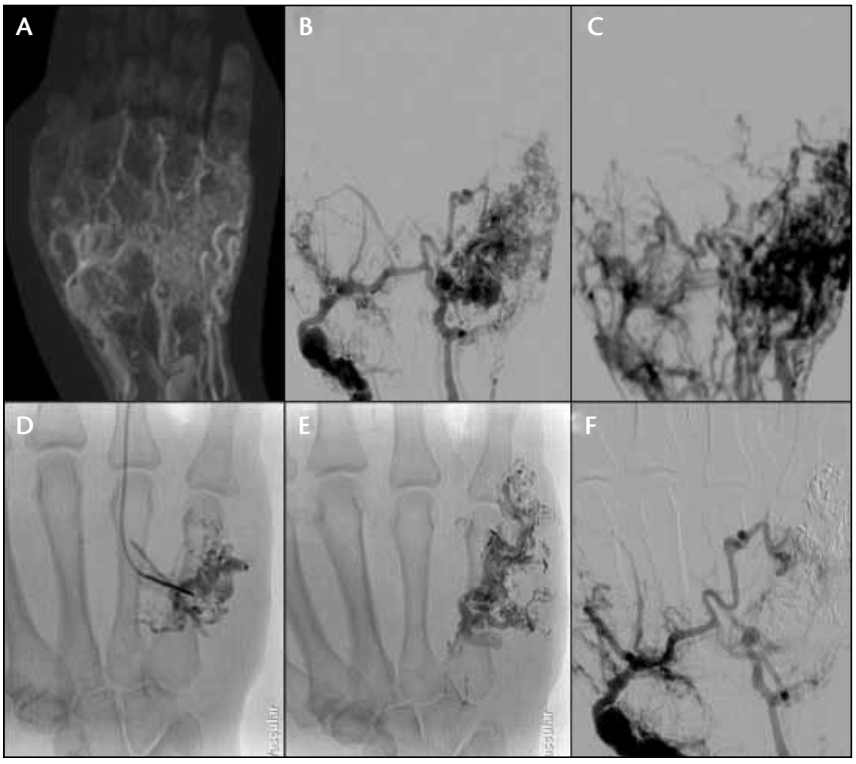

Figure 4. A 33-year-old woman presented with a long-standing history of left hand AVM with pain and episodes of numbness, as well as cosmetic issues. The patient was seen by multiple physicians who thought treatment would be high risk. MRA and upper extremity catheter angiography demonstrated a hypothenar AVM (A through C). Due to the marked tortuosity of the feeding arteries, the nidus was accessed with direct puncture using a 21-gauge butterfly needle (D). Panel E demonstrates the embolic agent cast. Final angiography demonstrated approximately > 80% reduction in the AVM (F). Four weeks after the treatment, the patient's symptoms had almost completely resolved.

the secured in place, and the procedure is repeated every day for 3 days. It is important to note that the treatment of microcystic lesions is challenging because these small cysts are difficult to access. The results for microcystic and combined lesions are not as good as for macrocystic lesions.

Similar to venous malformation, several sclerosing agents have been used in the treatment of lymphatic malformations. Ethanol, STS, doxycycline, bleomycin, and OK-432 have been used. Currently, the preferred agents are doxycycline and bleomycin due to their excellent results in macrocystic lesions and their safety profile. Acevedo et al performed a literature review of nonsurgical treatments for head and neck lymphatic malformations. Their results revealed that 66.5% of patients who received OK-432 for lymphatic malformations achieved a complete/excellent or good response, 16.9% achieved a fair/poor response, and 15.4% observed no response. The results of patients treated with bleomycin showed 72.3% excellent or good response, 18.4% fair/poor response, and 11.6% no response. Seven major complications were noted out of the 289 patients in the series.[28] Similar results were seen with bleomycin in series by Sainsbury et al, although the number of patients with lymphatic malformations who received treatment was small (n = 5).[5]

In the series by Yang et al, 65 patients with lymphatic malformations were treated with bleomycin. Thirty-two lesions (49%) were macrocystic, 30 (46%) were microcystic, and three (5%) were combined. Twenty-six of 32 macrocystic lesions (81%) showed > 90% reduction, whereas another six (19%) exhibited 50% to 90% reduction. Nineteen of 30 microcystic lesions (63%) showed > 90% reduction, 10 (33%) had 50% to 90% reduction, and one (4%) had < 50% size reduction. Of the three combined lesions, two (67%) had > 90% shrinkage, and one (3%) had < 50% reduction.[29] Doxycycline is usually administered in a concentration of 10 mg/mL, with a maximum dose of 1,000 mg.[4,12,16] In a series by Burrows et al, 41 patients were treated with doxycycline (49% macrocystic, 44% combined, and 7% microcystic) in a total of 60 procedures. They reported a 2% major complication rate and a 10% minor complication rate. Treatment response was excellent for macrocystic lesions, good for combined lesions, and fair/good for microcystic lesions.[12]

In a series of 11 patients treated with doxycycline, all seven patients with macrocystic lesions achieved complete clinical resolution, with an average radiographic resolution of 93%. Four patients who had mixed lesions achieved only partial clinical resolution and an average of 73% radiographic resolution. None of the patients experienced any adverse effects related to the treatment. At a median follow-up of 8 months, two patients (18%) experienced lesion recurrence in the setting of concomitant infection.[30]

HIGH-FLOW VASCULAR MALFORMATIONS: AVMS

AVMs pose a very difficult therapeutic challenge. They are locally aggressive lesions that can present in several different ways, from completely asymptomatic lesions to significant bleeding, pain, neuropathy, or congestive heart failure.[6-9,20,31-36] A diagnosis can be made based on clinical history and confirmed with Doppler ultrasound and MRI and contrast-enhanced MR angiography.[8,9] Catheter angiography is still considered the gold standard in the evaluation and treatment planning of these lesions because it provides detailed information of the angioarchitecture, with great spatial and temporal resolution.[7] AVMs are uncommon lesions that require significant expertise for successful treatment. Several therapeutic strategies have been proposed, including surgery, embolization, or a combination of both.[6-9,20,31-36] Many times, even in experienced hands, complete cure is not possible, thus control of symptoms is the aim of treatment.

Whenever possible, the goal of interventional treatment should be complete occlusion of the nidus or fistulous connections (Figure 3). Transarterial access can be used, and the microcatheter should be advanced to a location as close to the nidus/fistulous connections as possible. Super-selective microcatheter contrast injection should be performed. It is important to understand the angioarchitecture of the lesion, including the presence of supply to normal tissue, venous drainage, and transit time, as well as reflux into the feeding arteries.

If supply to normal tissue is seen, embolization at that location should be avoided if possible. This can be achieved by advancing the microcatheter to a more distal location. Proximal endovascular occlusion (which does not reach the nidus) with embolic agents, such as coils, should also be avoided because they would only close the access to the nidus without providing any true AVM treatment. If the transit time is very fast, embolization should be performed carefully. Temporary compression or permanent occlusion of the outflow veins can be performed to aid embolization by decreasing the flow transit time.

In cases when the transarterial route cannot be used due to severe tortuosity or proximal occlusion from previous embolization or surgical procedures, direct puncture can be performed using ultrasound guidance or transarterial roadmap images obtained from catheter angiography (Figure 4). Small 21- to 23-gauge needles are usually used. Contrast injection is performed to confirm the position of the needle in the nidus. The same principles then apply as with transarterial embolization. On some occasions, there is a single-outflow venous sac that works as a collector for all of the multiple arterial feeders. In these cases, transvenous catheterization or direct puncture of this venous collector should be performed instead of the transarterial approach because occlusion of the venous collector will cure the AVM.[9,32]

Embolic agents with different properties have been used in the interventional treatment of AVMs. Coils, ethanol, Trufill n-BCA, and Onyx have been used in the treatment of high-flow AVMs. It is important to learn about the technical particularities of each agent, which have been described elsewhere.[6-9,20,31-36] Of all the embolic agents, ethanol seems to be the one associated with the highest degree of successful permanent occlusion, even in extensive lesions. However, due to its known complications (ranging from skin blistering to neuropathy and, in extreme cases, cardiopulmonary collapse and death), it should be used by physicians who have experience with this agent.[6-9,31,33,34]

Other embolic agents like Trufill n-BCA and Onyx have been successfully manage high-flow AVMs alone or in combination with surgery.[10,20,35,36] These embolic agents are effective in controlling symptoms such as hemorrhage, as well as palliative measures, and their safety profile seems more favorable compared to ethanol. However, complete clinical resolution is difficult in cases of extensive lesions and sometimes even in localized lesions requiring surgical resection for better results.[10,20,35,36]

CONCLUSION

In summary, vascular malformations are a challenging group of entities that can be successfully managed with interventional techniques. It is important for the physicians who treat these complex patients to be familiar with the different approaches, techniques, and sclerosing and embolic agents that can be used, so that these patients can be offered the best available treatment for each specific case. ■

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