

Vascular Malformations: Effective Treatment with Absolute Ethanol

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SCOPE OF THE PROBLEM

Vascular malformations are extremely challenging lesions. The clinical presentations of these congenital abnormalities are protean and range from asymptomatic birthmark to life-threatening congestive heart failure or exsanguinating hemorrhage. These abnormalities are rare; most clinicians will see only a few in a lifetime of practice. Thus patients afflicted with these disorders often seek help from many different physicians and undergo repetitive examination, diagnosis, and frequent failed attempts at "definitive" therapy leading to exacerbation of symptoms, lesion recurrences, and disability (1).

Vascular anomalies were first treated by surgeons. The early surgical paradigm of proximal arterial ligation of arterial feeders proved futile when the phenomenon of neovascular recruitment rapidly reconstituted arterial inflow to the AVM and as microfistulous connections became macrofistulous feeders. Complete extirpation of an AVM nidus proved very difficult and very hazardous in that massive hemorrhage often occurred. Partial resections could cause an initial good clinical response but with time the patient's symptoms usually recurred or worsened. Over time, it became apparent to vascular surgeons that, as stated by D.E. Szilagyi, M.D., ".with few exceptions, their cure by surgical means is impossible. We had intuitively thought that the only answer of a surgeon to the problem of disfiguring, often noisome and occasionally disabling blemishes and masses, prone to cause bleeding, pain, or other unpleasantness was to attack them with vigor and with the determination of eradicating them". The results of this attempt at radical treatment were disappointing. In Szilagyi's series of 82 patients only 18 were felt to be operable and of those, 10 were improved, 2 were the same, and 6 were worse at follow-up (2).

As the discipline of interventional radiology developed, the treatment of these lesions by embolization with particulate matter became widely used either as an attempt to completely destroy the lesion, control flow (and therefore symptoms) or as a preoperative maneuver to reduce blood loss and allow complete removal (3, 4, 5). Over time, however, it was found that with rare exceptions complete destruction or "cure" of an arteriovenous malformation with particulate embolotherapy was rare. Despite the use of small particles and marked improvement in catheter delivery systems, the use of mechanical occlusive agents was ultimately a disappointment for us and others. The

vast majority of AVMs recurred after embolization via the same phenomenon as recurrences after surgery: neovascular recruitment with reconstitution of arterial inflow into the arteriovenous malformation nidus

Liquid agents such as tissue glues, alcohol, and sodium tetradecyl sulfate (Sotradecol) had been sparingly used as vascular occlusive agents by interventional radiologists for a number of years including use in the liver, bronchial arteries, and kidneys (6, 7). Sodium tetradecyl sulfate had also been commonly used to treat superficial venous varicosities with good results. The action of liquid embolic agents appeared to be mediated via a more potent and destructive mechanism than the simple vascular occlusion provided by particles but it was felt that intravascular liquids would be far too hazardous for general use. However, in 1986, Yakes et al described curative treatment of an extremity arteriovenous malformation with absolute alcohol (8). Since that time, it has become increasingly apparent that ethanol embolotherapy of vascular malformations can be curative, even in complex arteriovenous malformations. In this chapter, we discuss the use of alcohol to treat a variety of high flow and low flow vascular lesions. We believe that the use of alcohol offers significant promise for the patients afflicted with these disorders and now believe it to be the agent of choice for vascular malformation therapy (1, 9).

NOMENCLATURE OF VASCULAR MALFORMATIONS

Classification of vascular malformations has until recently been quite confusing. Authors and workers used inaccurate or ill-defined terms, such as cavernous hemangioma, venous angioma, cirroid aneurysm, congenital arteriovenous fistula, and many others. The lack of a standard nomenclature caused much diagnostic inaccuracy and confusion but the recent classification system of Mulliken and his coworkers has clarified the field a great deal. In this chapter we will use his system for dividing vascular malformations into hemangiomas (pediatric lesions) and malformations (venous, lymphatic and arteriovenous). These lesions can also be divided into high flow (arteriovenous malformations and arteriovenous fistulae) and low flow (venous malformations, lymphatic malformations, and mixed malformations) lesions (10). The term "hemangioma" should be used only for those lesions in children which become apparent during the first month of life rapidly proliferate and then slowly involute spontaneously to almost complete resolution at a young age (4 to 7 years old). In adults, the term "hemangioma" should not be used since these are not truly hemangiomas and rather venous malformations. Port wine stains (which have previously been called "capillary hemangiomas") should be called "capillary malformations". Additionally, descriptions of congenital syndromes often use inappropriate terminology to characterize the vascular lesions associated with them. Whenever possible these descriptions should also be replaced with the more accurate terms noted above.

IMAGING OF VASCULAR MALFORMATIONS

Imaging of vascular malformations is vitally important since these lesions are by definition more extensive and infiltrative than they may initially appear. Until recently, arteriography and venography were the sole methods of assessment and while the information obtained from these techniques remains initially important (we never treat a lesion without careful selective and superselective arteriography or venography), cross sectional imaging has assumed preeminence in the identification, characterization, and localization of vascular malformations. Two modalities in particular, color Doppler ultrasound and magnetic resonance imaging (MRI), have assumed a dominant role in imaging of these lesions.

MRI

In our experience, magnetic resonance imaging is the definitive tool for cross sectional imaging of vascular malformations. Rak et al identified and characterized the MR appearance of malformations, including venous malformations, arteriovenous malformations, and arteriovenous fistulae and showed that MRI was essential in separating vascular lesions into high flow and low flow types (11). The predominant distinction between venous malformations and arteriovenous malformations and fistulae is on T2-weighted MR images. On these sequences, venous malformations are of very high signal intensity ("bright"). Arteriovenous fistulae and arteriovenous malformations demonstrate little or no signal due to the phenomenon known as "flow void". In addition, magnetic resonance imaging shows involvement of neural, subcutaneous, and/or muscular structures due to its superior tissue differentiation. The multiplanar imaging capabilities of MRI also allow localization and characterization of complex lesions whether truncal or extremity in location.

Regarding computed tomography (which we have used in the past), we have found that magnetic resonance imaging is superior in virtually all aspects to CT and except for specific situations, we have abandoned the use of computed tomography in the work-up and evaluation of vascular malformations.

Color Doppler Ultrasound

Color Doppler ultrasound has also been very useful in identifying both high-flow and low-flow vascular lesions. We have also found this technique essential in guiding direct puncture of malformations by permitting accurate localization of the nidus. Follow-up examination is commonly used to document the decreased vascular flow rates and thromboses that occur after successful therapy.

ETHANOL AS A VASCULAR OCCLUSIVE AGENT

Ethanol is a powerful sclerosing agent that denatures blood proteins and destroys vascular endothelial cells by dehydration and denudation. These changes (which essentially cause tissue necrosis and death) occur rapidly and cause thrombosis

of the malformation. In malformations, these changes are desirable and account for the curative effects of this therapy. It is obvious, however, that the use of ethanol in a normal vascular structure is to be eschewed as introduction into vessels supplying structures such as nerves, muscles, or connective tissue will result in necrosis of that tissue. Ethanol treatment of vascular malformations thus requires significant experience with the agent, as well as extreme caution and a complete understanding of the pathophysiology of the vascular malformation being treated. It should be stressed that patients with vascular malformations are some of the most problematic and complex cases seen by vascular specialists. We believe that these abnormalities should only be treated at medical centers where such patients are seen regularly. In an average practice (even a busy one), only a handful of vascular malformations will be seen over the course of a career and it is in those cases that the injudicious or inappropriate use of alcohol is most hazardous since the agent necessary to produce a cure can also produce severe complications.

Safe Use of Ethanol in Vascular Malformations

Technical intraprocedural requirements for the use of ethanol include the following: 1) Superselective catheter placement or direct deposition of ethanol within the nidus of the vascular lesion. 2) Avoidance of alcohol injection into normal vessels. 3) Use of general anesthesia with appropriate intraprocedural monitoring. 4) Good immediate postoperative care including appropriate use of medications to reduce sequelae of any side effects. 5) Careful clinical follow-up with appropriate re-do therapy when necessary to produce maximum benefit

The application of the above-mentioned principles permits treatment of specific types of vascular lesions. In the next section we discuss how alcohol can be used effectively and safely in various malformations.

Ethanol Treatment of Venous Malformations

Venous malformations are congenital lesions which present with a variety of abnormalities ranging from relatively focal, contained vascular lesions to infiltrating vascular abnormalities with multiple venous channels. Venous malformations generally present with pain as a predominant symptom although they may cause tissue ulceration or induce changes in adjacent bones. Cosmetic deformities, particular in head and neck venous malformations, are also important issues. In the extremities, venous malformations usually produce pain and frequently induce swelling of an extremity; venous ulcerations may also appear (10).

Arteriography inevitably demonstrates normal size and flow in the arteries; there may be minimal contrast pooling within the abnormal venous structures on late phase films. For this reason, arteriography is generally a poor way to identify venous malformations. In our experience, the procedure of choice for identification of venous malformations is

magnetic resonance imaging which shows the lesions to be very bright on T2. Other mandatory work-up includes closed system venography and/or direct-puncture venography which better demonstrates the size and volume of the venous malformation. Color Doppler ultrasound is also useful in work-up.

The treatment of venous malformations epitomizes the successes that we have achieved with ethanol sclerotherapy in that the majority of lesions can be successfully ablated with alcohol. Venous malformations are inevitably best treated by direct percutaneous puncture to directly access the abnormal venous elements. The venous malformation is carefully evaluated at the time of therapy for total volume and through the above-mentioned concepts of flow occlusion and compression. The volume of contrast needed to fill the lesion is assessed repeatedly. During that assessment avoidance of flow into normal veins is paramount; once the appropriate volume and pressure relationships are achieved, injection of ethanol in the desired volume is performed. Postoperative complications are generally minimal although we have seen neuropathy and skin ulceration (13).

We believe that the majority of venous malformations can be cured or considerably reduced in size (to an asymptomatic level) by the use of ethanol therapy. We use follow-up MRI frequently; it inevitably demonstrates absent signal in an area that previously showed intense signal on T2. This appearance documents the destruction and complete thrombosis of the venous malformation.

Ethanol Treatment of Arteriovenous Malformations (AVM)

Arteriovenous malformations are congenital lesions in which abnormal primitive communications exist between artery and vein. The central and significant feature of an arteriovenous malformation is the presence of a primitive vascular nidus which rapidly empties into dilated tortuous outflow veins without the presence of a normal capillary bed. The symptoms associated with arteriovenous include high output cardiac failure, disfigurement, pain, neuropathy, exsanguinating hemorrhage, and venous hypertension, particularly when the malformation is located in a limb. In these patients, ulceration related to venous hypertension is a chronic and problematic issue and is often the symptom that leads to contact with a physician. Mulliken has characterized the effects of arteriovenous malformations as predominantly related to vascular shunting through the malformation. These effects include: 1) increased flow in the inflow artery with dilatation, thickening, and tortuosity. 2) Parasitic flow through the fistula which causes reversal of normal flow in the distal arterial segment. 3) Lowering of distal arterial pressure with production of ischemia in the structure supplied. 4) Increase in peripheral venous pressure which accentuates the peripheral arterial ischemia and precipitates pain, ulceration, edema, and gangrene. 5) Increased cardiac output with subsequent development of heart failure (1). These reasons and usually mandate the ultimate treatment of arteriovenous malformations, although we have seen relatively asymptomatic AVMs in patients as old as 65 years.

Treatment requires superselective catheterization or direct puncture of the nidus in order to prevent complications of inadvertent nontarget embolization. Inflow or outflow occlusion is generally required to produce vascular stasis. Another important principal is the use of staged or multiple procedures. However, when appropriately utilized, alcohol ablation of AVMs can be curative. The use of ethanol has led us to conclude that the possibility of cure even in complex or large lesions can be now legitimately discussed with many patients. While cure is not always possible in every patient, ethanol therapy can often reduce flow in and size of the lesion to a point where symptoms are not present, a limb is saved or cardiac output is reduced to reasonable levels, thus avoiding the long-term problems associated with high output through such fistulous lesions.

On the other hand, the use of alcohol in arteriovenous malformations raises the stakes considerably as far as complications are concerned. These high flow lesions can be difficult to localize and/or catheterize and the risk of nontarget embolization remains relatively high. Neural ischemia is our most feared complication but we have also observed pulmonary embolism during treatment of large fistulous AVMs. Currently, our combined complication rate for arteriovenous malformation therapy is 15 percent with the majority of these complications being self limited and reversible, although permanent neural ischemia and neuropathy has certainly been observed. Despite these potential problems, we remain extremely encouraged about the use of ethanol and believe it to be the only agent which should be used in arteriovenous malformations (1, 9). We believe strongly that conventional occlusive embolic agents such as polyvinyl alcohol particles, Gelfoam pledgets, glue or coils should never be used because of the inevitable recruitment of collateral vessels and neovascularity which either exacerbates symptoms or makes appropriate treatment with ethanol more difficult by limiting access to major vascular channels.

Ethanol Treatment of Pediatric Hemangiomas.

Pediatric hemangiomas are self limited lesions. It should be obvious then that these lesions usually do not require treatment. On the other hand, under rare circumstances therapy may be warranted when such unusual problems such as congestive heart failure or the Kasabach-Merritt syndrome occur. The Kasabach-Merritt syndrome is a consumptive coagulopathy secondary to platelet trapping which produces systemic bleeding complications. In general, steroids or alpha-interferon will treat this problem effectively but we have seen some situations in which medications were not effective and direct alcohol injection into the malformation was necessary to stabilize the patient. In other areas, pediatric hemangiomas may cause compression upon vital structures such as the airway or may cause visual disturbances when located in and around the eye. In such cases, the need for treatment and alleviation of symptoms must be balanced against the knowledge that the lesion will inevitably involute. In these

cases of pediatric hemangioma, treatment with ethanol is performed in a similar manner to treatment of venous malformations.

Ethanol treatment of arteriovenous fistulae.

Congenital and post-traumatic arteriovenous fistulae are interesting lesions. For the most part, large fistulae which occur traumatically can be treated readily by surgery or embolization but in some situations chronic arteriovenous fistulae can be confused with arteriovenous malformations at both arteriography and MRI because the multiple inflow arteries can simulate an AVM. These lesions may mimic AVMs in terms of complications and deficits. Treatment of arteriovenous fistulae is unlike the other lesions mentioned here in that cure can be accomplished with other agents besides ethanol including balloons, glue or coils but these lesions must be treated by closing the fistula directly and not the feeding vessels as we have seen a number of situations in which incomplete closure by surgical ligation or inappropriate embolization causes recanalizations and recurrences. In some circumstances, ethanol can also be successfully used agent for the management of arteriovenous fistulae (14).

Conclusion

Alcohol therapy of vascular malformations is a challenging, difficult but ultimately rewarding pursuit. Over the past 10 years, we have learned a great deal about appropriate imaging work-up and pathologic classification of these lesions. We believe that many venous malformations and AVMs can now be considered curable with the use of alcohol sclerotherapy. In other lesions, alcohol offers considerable promise of lesion control and improvement of symptoms. Alcohol embolotherapy can, however, produce significant morbidity and we, therefore, strongly advise that these lesions be treated by an interventionalist possessed of significant knowledge and skill. Ethanol ablation of vascular malformations is, we believe, now the preferred technique for the management of these extremely complex and challenging lesions.

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