RadioGraphics

Peripheral Vascular Malformations: Imaging, Treatment Approaches, and Therapeutic Issues[1]

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CME FEATURE

See accompanying test at http://www.rsna.org/education/rg_cme.html

LEARNING OBJECTIVES FOR TEST 5

After reading this article and taking the test, the reader will be able to:

- Identify the current roles of imaging modalities in the evaluation of peripheral vascular malformation.
- Discuss therapeutic approaches for peripheral vascular malformation, focusing on selection of sclerotic agents and their merits.
- Describe patient preparation to prevent complications and their treatment.

TEACHING POINTS

See last page

Peripheral vascular malformations are now described according to some accepted guidelines, and the principle of proper treatment (nidus ablation) is becoming clear. An appropriate classification scheme for vascular anomalies and definite indications for treatment are important to successful treatment overall. The findings from noninvasive imaging (ie, Doppler ultrasonography, computed tomography, or magnetic resonance imaging) in association with clinical findings are critical in establishing the diagnosis, evaluating the extent of the malformation, and planning appropriate treatment. Direct opacification of the nidus is useful, not only in making a correct diagnosis, but also in treating the lesion with sclerotherapy. In most cases, conservative treatment is recommended, but when a patient suffers clinical complications (eg, ulceration, pain, hemorrhage, cardiac failure, or unacceptable cosmetic consequences), the nidus sclerotherapy becomes mandatory. If the vascular malformation has blood outflow to a drainage vein during nidus opacification, flow control (with balloon occlusion, tourniquet, or embolization) is necessary to achieve sclerosant stasis within the nidus. Embolotherapy (with a coil, *n*-butyl cyanoacrylate, or small particles) should be used for subsequent multifaceted palliative therapy. A multidisciplinary approach is needed in the treatment of a high-flow lesion, and a dedicated team approach is necessary for appropriate management in most cases.

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Introduction

Peripheral vascular malformations are some of the most difficult lesions to diagnose and treat. Clinical manifestations vary from none to life-threatening congestive heart failure. Surgery has been the standard treatment, but functional or cosmetic problems sometimes follow surgical therapy. Percutaneous sclerotherapy for vascular malformations has yielded favorable results, although there is substantial variation among the techniques used and in the selection of the sclerosing agent. Herein, we describe our current approach to the diagnosis of vascular malformations as well as therapeutic approaches, focusing particularly on endovascular sclerotherapy.

Classification and Description of Vascular Malformations

Vascular (arteriovenous) malformations of the extremities constitute some of the most difficult diagnostic and therapeutic challenges. In 1982, Mulliken and Glowacki (1) proposed hemangioma and vascular malformations as two major categories of lesions based on histopathologic findings. In 1993, Jackson et al (2) proposed another system for classifying hemangiomas, vascular malformations, and lymphatic malformations on the basis of vascular dynamics. A classification system for vascular anomalies based on cellular features, flow characteristics, and clinical behavior was updated during the meeting of the International Society for the Study of Vascular Anomalies (Table 1) (3). In 1996, Kawanabe et al (4) reported a system for practical classification of vascular lesions in which the treatment procedure is selected according to the characteristic flow within the lesion (Table 2) (5).

Clinical Characteristics

Although vascular malformations are congenital, they may not be seen at birth. The main locations are the head and neck (40% of cases), extremities (40%), and trunk (20%) (6). Arteriovenous malformations, having no relation to endothelial proliferation, are caused by abnormal differentiation of the vascular system during embryogenesis. These lesions may not be evident until additional growth or vascular engorgement manifests as a response to thrombosis, trauma, infection, or endocrine fluctuations (2); thus, these evolutive vascular malformations rarely appear before adolescence (3). Unlike hemangiomas, vascular malformations generally increase proportionally in size as the child grows.

In contrast, more than half of hemangiomas are seen at birth. They have endothelial hyperplasia with increased endothelial turnover. They undergo an initial proliferative phase, and they finally involute with age (1,7,8). Unlike vascular malformation, most of the hemangiomas make invasive treatment unnecessary (9).

Pathologic and Genetic Features

Vascular malformations occur as a result of aberrant vessel angiogenesis. They are localized or generalized congenital vascular abnormalities comprising direct microscopic connections between arteries, veins, and lymphatic vessels without the normal capillary bed. The confluence of small tortuous vessels is called a *nidus*, where arteriovenous shunting occurs without a capillary bed. One malformation may contain multiple nidi.

Vascular malformations have a high recurrence rate because they originate from the mesenchymal cells at an early stage of embryogenesis. They retain the embryonic growth potential, which is often represented clinically as recurrence. Some vascular malformations become increasingly destructive as they continue to grow and progress.

Some vascular malformations appear as part of a familial genetic disorder called angiomatous syndrome. One form of this syndrome, Rendu-Osler-Weber syndrome, is caused by two genetic disorders (10,11), both of which result in the loss of function of cell receptors. Rendu-Osler-Weber syndrome usually manifests with telangiectasia of the skin and mucous membranes (mouth and gastrointestinal tract). The telangiectasia typically appears during puberty and causes bleeding (12). In addition, some of the vascular malformations are associated with a mutation in signaling for various growth factor receptors that control proliferation, migration, and survival of vascular endothelial cells (13,14).

Selection of Imaging Modalities

Multiple imaging modalities should be used to evaluate characteristics of the lesion, such as size, flow velocity, flow direction, relation to the surrounding structures (vessels, muscle, nerve, bone, skin), and lesion contents.

Conventional Radiography

Conventional radiography plays only a small part in the diagnosis and classification of vascular lesions, but it provides useful information about bone and joint involvement. Bone erosion, sclerotic change, periosteal reaction, and pathologic fracture each suggest bone involvement. Phleboliths are specific to hemangioma.

Table 1
ISSVA Classification of Vascular Anomalies*

Vascular Tumor	Vascular Malformation	
	Simple	Combined
Hemangioma	Capillary malformation	Arteriovenous fistula, arteriovenous malformation, capillary-venous malformation, capillary-lymphatic-venous malformation
Other	Lymphatic malformation	Lymphatic-venous malformation, capillary-lymphatic-arterio-venous malformation
	Venous malformation	

*ISSVA = International Society for the Study of Vascular Anomalies.

Table 2
Classification of Surface Vascular Lesions

Traditional classification
Capillary hemangioma
Strawberry hemangioma
Strawberry nevus
Port wine stain
Flame nevus
Cavernous hemangioma
Venous angioma
Lymphangioma
Arteriovenous malformation
Classification of Jackson et al*
Hemangioma
Vascular malformation
Low-flow lesion
High-flow lesion
Lymphatic malformation
Flow-related classification and recommended treatment
Slow-flow lesion: sclerotherapy
Intermediate-flow lesion: sclerotherapy (plus embolization)
High-flow lesion: embolization (plus sclerotherapy)

*Reference 2.

Ultrasonography

Ultrasonography (US) is an essential, noninvasive tool that is widely used to examine superficial vascular lesions. Color Doppler imaging permits real-time analysis of arterial and venous flow and measurement of flow velocities. It is an important method for monitoring patients who have undergone therapy, but it is limited in the assessment of deep lesions and lesions adjacent to interfering air or bone.

Computed Tomography

Computed tomography (CT) with intravenous contrast material is useful for assessment of vascular malformations. Multi–detector row CT can be a valuable means to evaluate the effect of enhancement, existence of calcification or thrombus, distal runoff (when lesions are located in the extremities), and concomitant lesions. The high temporal resolution of CT and the ease with which findings can be interpreted are advantageous in evaluating vascular lesions. However, because CT involves considerable exposure to ionizing radiation and provides less information about blood flow, magnetic resonance (MR) imaging has replaced CT in the evaluation of vascular malformations.

MR Imaging

MR imaging is the most valuable modality in the classification of vascular malformations. It depicts the anatomic relation between the vascular lesion and adjacent organs, nerves, tendons, and muscles. Slow-flow venous malformations have high signal intensity on T2-weighted images, whereas high-flow arteriovenous malformations and fistulas contain a signal void. Phleboliths and calcification also show signal voids with all image sequences. Dynamic study with a gradient pulse sequence is useful for evaluating the flow velocity (slow, intermediate, or high) of lesions and in monitoring patients who have undergone therapy.

Phlebography and Angiography

Phlebography (direct nidus opacification) and angiography are important not for preoperative assessment but together as a precursor to interventional procedures such as sclerotherapy and embolization, despite the fact that they are invasive and painful and involve exposure to radiation. With the use of direct puncture of the nidus, its volume and flow pattern can be evaluated (15).

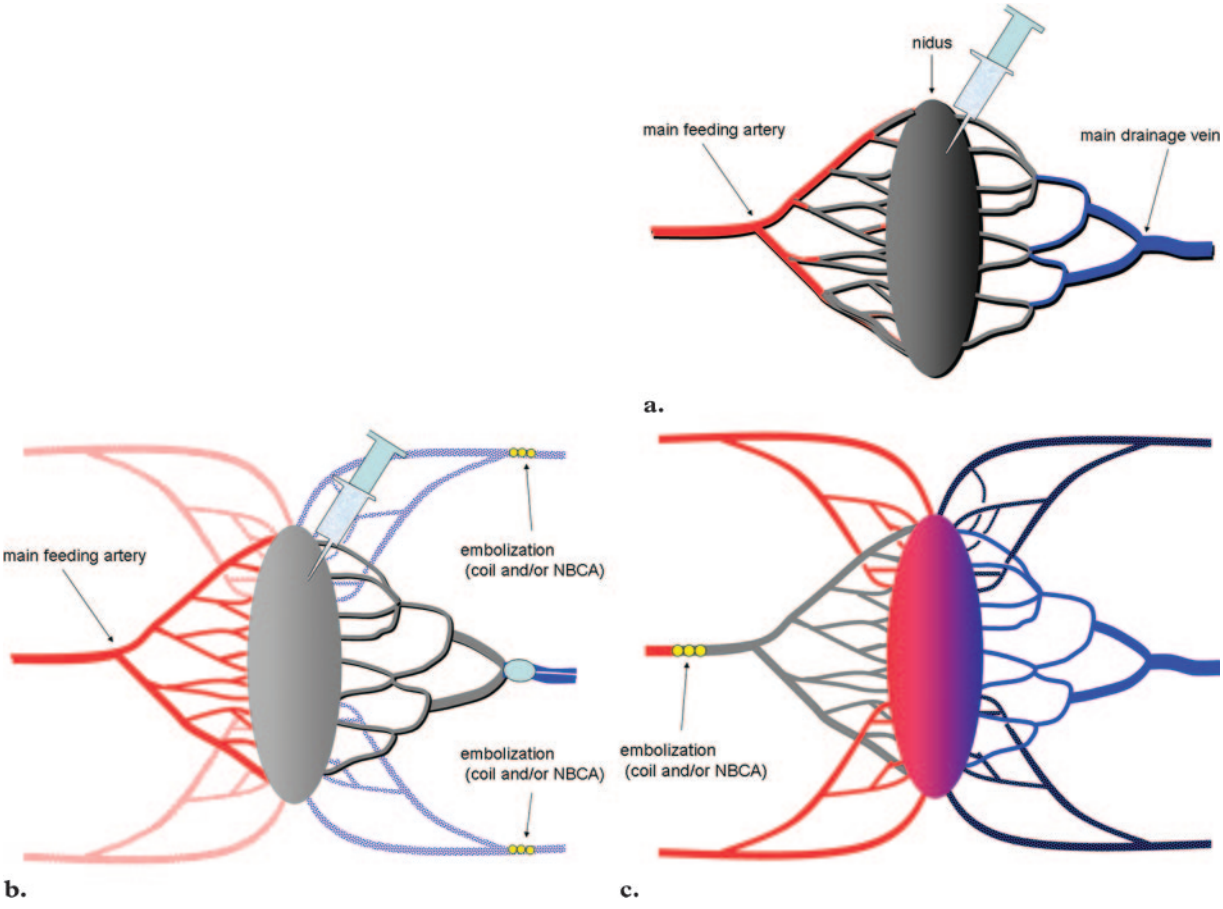


Figure 1. Treatment of vascular malformation. **(a)** Diagram shows a simple vascular malformation that consists of one feeding artery, the nidus, and one drainage vein. For this type of lesion, sclerotherapy with percutaneously administered liquid sclerosant is indicated. **(b)** Diagram shows a vascular malformation with several feeding arteries and drainage veins. For this type of lesion, sclerotherapy begins with a flow-control procedure (the drainage vein is occluded by means of a balloon catheter with or without use of coils or *n*-butyl cyanoacrylate [*NBCA*] to decrease the number of drainage veins) to achieve sclerosant stasis. Additional sclerotherapy to the nidus is then performed. **(c)** Diagram shows a vascular malformation with several drainage veins and feeding arteries, one of which was embolized. This is an ineffective procedure that makes the latent feeding arteries apparent. The nidus flow volume usually increases, and clinical symptoms worsen. As with embolization of the feeding artery, coil embolization of the drainage vessel alone is not sufficient treatment. Without ablation of the nidus, a good outcome cannot be expected.

Principles and Selection of Treatment

Teaching Point

Because vascular malformations are responsive to various stimuli such as injury and surgical intervention, improper treatment often rapidly stimulates quiescent vascular malformations, making the condition worse. Feoktistov et al (16) reported that hypoxia modulates the expression of adenosine receptors in human endothelial and smooth muscle cells toward an angiogenic phenotype. Therefore, complete destruction of the nidus of a vascular malformation is the only potential cure (Fig 1). Ameliorating the clinical symptoms can be another goal in treating problematic vascular malformations (17). Clinical improvement can be achieved with several courses of sclerotherapy (18).

Embolizing or sclerotic agents, such as absolute ethanol, polidocanol (Aethoxysklerol; Kaigen, Osaka, Japan), ethanolamine oleate (Oldamin for injection; Grelan Pharmaceutical, Tokyo, Japan), *n*-butyl cyanoacrylate (Histoacryl; B. Braun, Melsungen, Germany), various types of coils, polyvinyl alcohol foam powder (Ivalon; Cook, Bloomington, Ind), and superabsorbent polymer microspheres (19), have been used in various combinations, simultaneously or in stages, depending on the location, severity, and extent of the vascular malformation (Table 3). Sclerotherapy in particular is accepted as independent therapy for vascular malformations. It has also been implemented as a preoperative or

Table 3
Advantages and Disadvantages of Sclerosants

Sclerosant	Advantages	Disadvantages
Absolute ethanol	Strong endothelial damage, high response rate, less expensive, easy to obtain	Painful during procedure, high complication rate, penetrative effect on deep vascular layer
Ethanolamine oleate	Excellent thrombosing effect, chemical damage to vessel wall, less toxic effect than absolute ethanol	May induce acute renal failure due to hemolytic effect, less endothelial damage than absolute ethanol
Polidocanol	Overhydration of endothelial cells, nearly painless procedure	May induce reversible cardiac arrest

postoperative adjunct therapy. It has helped improve surgical results and expanded the role of surgical therapy. The flow of vascular malformations can be reduced by means of embolotherapy, but such treatment is usually palliative, because a vascular malformation is in fact a malformative field with multiple arteriovenous fistulas (3). Although embolotherapy is generally a safe procedure in experienced hands, it should not be performed unnecessarily, particularly if the symptoms are not severe (20).

Teaching Point

Absolute Ethanol

Absolute ethanol is one of the main agents used in the treatment of surgically inaccessible lesions (17). It is administered via transarterial, transvenous, or direct-puncture injection, depending on the anatomic or hemodynamic status of the individual vascular malformation. The presence of ethanol in vessels causes endothelial damage, denaturation of blood proteins, thrombus formation, and vascular occlusion (17). A 64%–96% response rate, defined as improvement in symptoms or reduction in the size of the lesion, has been reported after ethanol sclerotherapy of venous malformations (21,22). Complication rates ranging from 7.5% to 27.9% have been reported (23–27); complications include minor skin blisters, skin necrosis, transient pain, muscle contracture, motor or sensory nerve injury (related to the swelling involved with resultant nerve compression rather than nontarget embolization of the vasa nervorum [28]), superficial cellulitis, deep vein thrombosis, pulmonary embolus, and cardiopulmonary collapse. Systemic alcohol contamination may also occur during sclerotherapy (29).

Ethanolamine Oleate

Ethanolamine oleate (used in 5%–10% of cases) is another of the main agents used for sclerotherapy (4,24,30). A salt of an unsaturated fatty acid, ethanolamine oleate is used as a sclerosing agent because it has excellent thrombosing properties. It is used commonly for the treatment of esophageal and gastric varices, and it should be mixed with nonionized contrast material to maintain a nonionic surfactant effect and achieve good visualization with fluoroscopy. Ethanolamine oleate is heavier than blood and has a tendency to sink within the cavity. Injection into varices leads to thrombogenesis as a result of chemical damage to the vascular wall (31). Varices show atrophic changes after intravariceal injection of ethanolamine oleate, even though the sclerosant remains in the vessels for only a few minutes (32). A hemolytic effect, visualized as red urine, occurs when the sclerosing agent leaks to the outside of the lumen. In cases in which it may be necessary to inject an overdose of ethanolamine oleate, prophylactic haptoglobin (2000–4000 U/h) (33) and albumin (>3.0 g/dL) (34) should be given before injection to prevent permanent renal insufficiency. Compared with ethanol, ethanolamine oleate has less effect on the deep vascular layer (and no penetrative effect); thus, it is not associated with neurologic side effects despite the proximity of the nervous system to the vascular system (30).

Teaching Point

Polidocanol

Polidocanol is generally used for sclerotherapy of esophageal and lower limb varices (35–38). It consists of 95% hydroxypolyethoxydodecane, and its detergent action induces rapid overhydration of endothelial cells, leading to vascular injury. Polidocanol sclerotherapy is a nearly painless procedure because polidocanol has an anesthetic effect; thus, general anesthesia is not necessary (35,37,38). Reversible cardiac arrest was reportedly induced by injection of 4 mL of 1% polidocanol to treat venous malformations in the legs of a 5-year-old child (39). In proportion to the

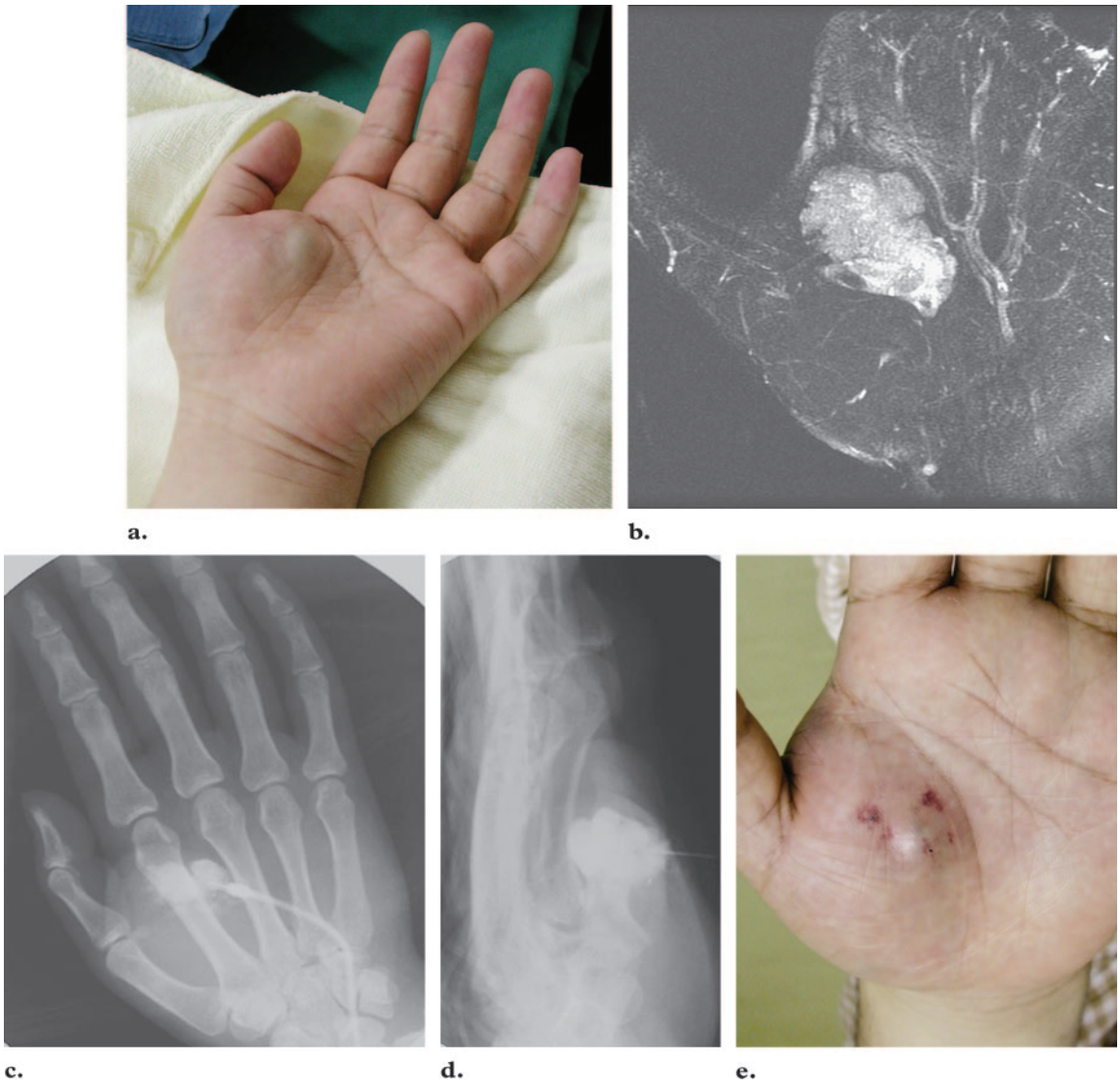


Figure 2. Slow-flow vascular malformation in a 33-year-old man with pain in the left palm and thumb. **(a)** Photograph demonstrates a blue lesion that protrudes from the thenar eminence. **(b)** Coronal fat-saturated T2-weighted MR image with maximum intensity projection shows a high-signal-intensity mass. **(c, d)** Images obtained during sclerotherapy show direct injection of ethanolamine oleate, which was performed after the maximum dose was determined and with intermittent fluoroscopic guidance. **(e)** Photograph obtained 2 days after sclerotherapy shows internal hemorrhage in the puncture sites, but protrusion of the lesion and clinical symptoms have decreased.

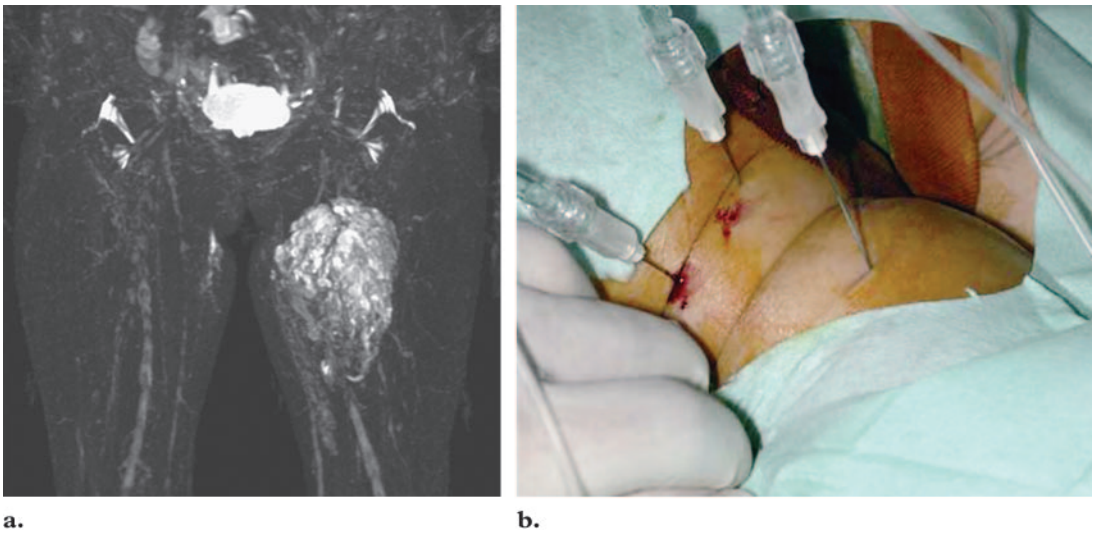
amounts present in the blood, local anesthetics reduce the electrical excitability of and conduction rate through the heart and depress spontaneous pacemaker activity in the sinus node, resulting in progressive sinus bradycardia and eventual sinus arrest (39).

The authors mainly use ethanolamine oleate; depending on the lesion, absolute ethanol or polidocanol is used in addition or as an alternative. Because there is no convincing evidence of permanent damage to the endothelium, embolic materials (eg, coils, *n*-butyl cyanoacrylate, small particles) should be used for subsequent multifaceted treatment of vascular malformations that includes, for example, flow reduction and control of bleeding (22,40).

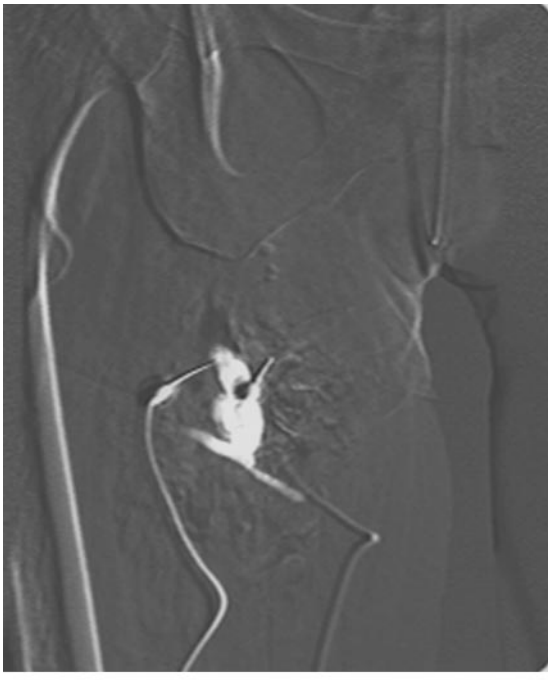
Method for Sclerotherapy

Preoperative image analysis (US, CT, and MR imaging) is used to determine the location of the nidus and estimate the flow velocity. A localized, slow-flow nidus is the simplest to treat; a large, high-flow nidus is the most difficult and requires a multidisciplinary approach. Before nidus sclerotherapy, transarterial or venous embolization at the feeding or drainage vessel is often helpful to

Teaching Point



a. b.



c.

Figure 3. Slow-flow vascular malformation in a 45-year-old woman with left thigh tenderness. **(a)** Coronal fat-saturated T2-weighted MR image shows a high-signal-intensity mass. **(b, c)** Intraoperative photograph **(b)** and angiogram **(c)** were obtained during sclerotherapy, which was performed with intermittent fluoroscopic guidance. Polidocanol was injected directly, but the sclerosing agent drained into the vein, and flow stasis was difficult to achieve within the nidus. Thus, multiple needle punctures were needed to distribute the sclerosing agent. After the procedure, the patient experienced reversible low blood pressure because of the anesthetic effect of polidocanol.

decrease the nidus inflow and effect stasis of the ablation material within the nidus.

Preoperative Anesthesia

A nerve block or local or general anesthesia is commonly used for sclerotherapy. Therapy with ethanol or ethanolamine oleate in particular causes tissue dehydration, damage to the inner lumen of the vessel, and vessel occlusion due to blood coagulation. It is necessary to administer a nerve block or local or general anesthesia because of the severe pain that occurs during the procedure, and a nerve block, local anesthetic, or narcotic or nonnarcotic anti-inflammatory drug is needed to relieve the pain for a few days after the procedure.

Injection Procedure

Before injection of the sclerosant, the physician should check the rate of blood flow (flow velocity) in the nidus. For sclerotherapy, percutaneous needle insertion is recommended (Fig 1); the approach route to the nidus should be determined according to preoperative images or imaging guidance (9). If it is impossible to reach the nidus for some reason, a transarterial, transvenous, or transosseous (41) approach is recommended. The physician should be aware that the injection should be in the nidus or as near to it as possible.

A slow-flow vascular malformation can usually be successfully treated with sclerotherapy (Figs 2, 3). If the approach route is free from severe complication, direct puncture with an 18–22-gauge needle is recommended. For a small lesion (≤30 mm in diameter), only one session is necessary to complete the procedure. Even for treatment of a vascular malformation without flow, careful gradual injection (with a 1.0–2.0-mL syringe) with fluoroscopic guidance is needed to prevent overdose and overflow into the drainage vein.

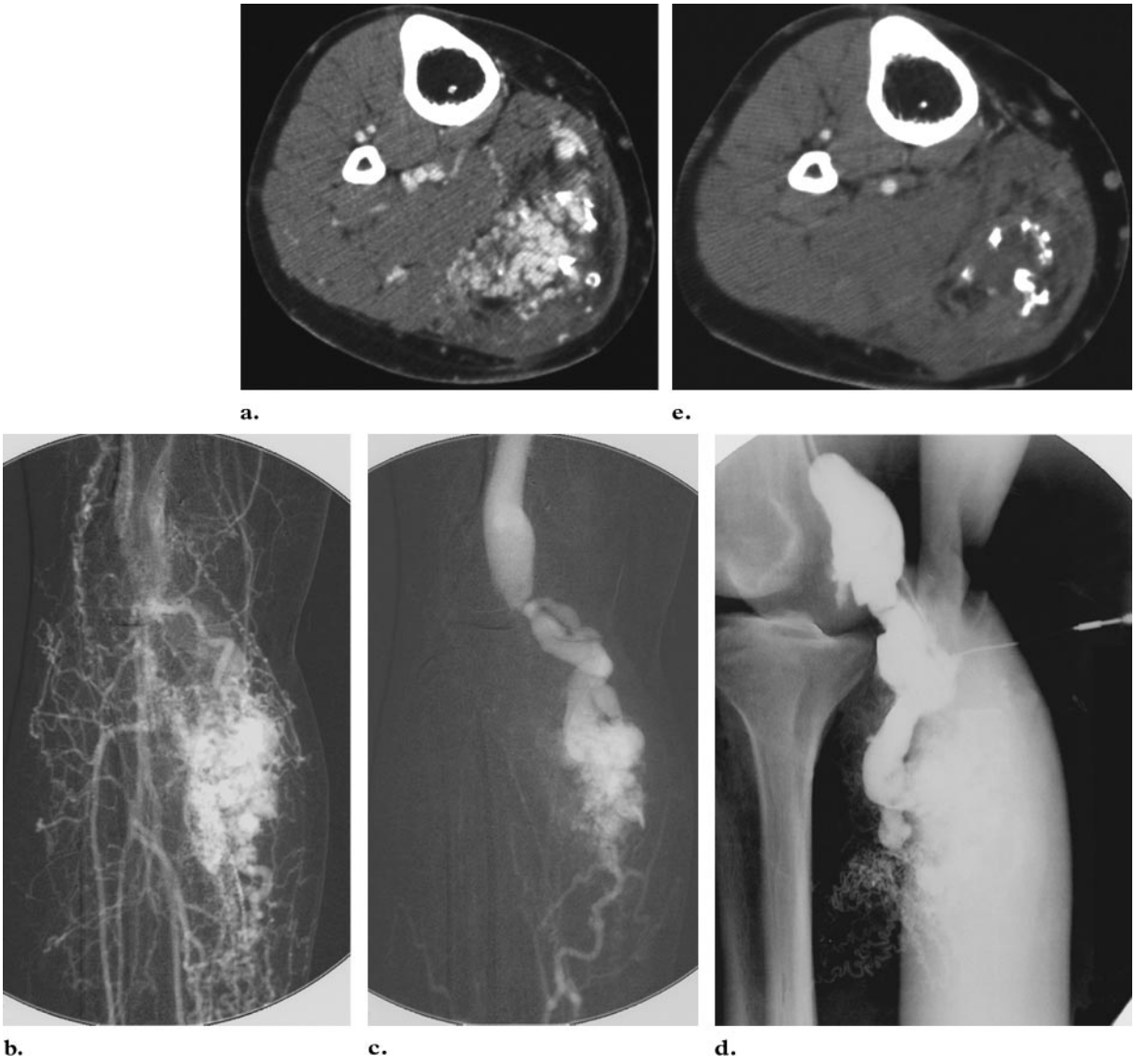


Figure 4. High-flow vascular malformation in a 22-year-old man with tenderness of the right lower limb. **(a)** Axial CT scan obtained with contrast material enhancement shows dilated vessels within the gastrocnemius muscle. **(b, c)** Angiograms show multiple feeding arteries and early venous return, findings that indicate a high-flow venous malformation. **(d)** Image obtained during percutaneous direct injection sclerotherapy. Balloon occlusion was performed at the popliteal vein, and 40 mL of ethanolamine oleate with 10 mL of absolute ethanol was injected into the nidus. Distribution of the sclerosant within the nidus (and the feeding artery retrogradely) is key to the success of the procedure. **(e)** Axial contrast-enhanced CT scan obtained at 2 years follow-up shows a thrombosed and diminished nidus.

Vascular malformations with an intermediate flow rate can usually be managed with sclerotherapy by using flow control such as by balloon occlusion, tourniquet, or coil or *n*-butyl cyanoacrylate embolization. The time for reaction between the inner surface of the nidus and the sclerosant can be extended by reducing the amount and rate of blood flow through the nidus. The dilution effect is thus minimized, increasing the success rate. After implementation of flow-control procedures, the injection method recommended for slow-flow vascular malformations is also recommended for intermediate-flow lesions.

High-flow (and diffuse) lesions are the most difficult of the vascular lesions to treat (Fig 4).

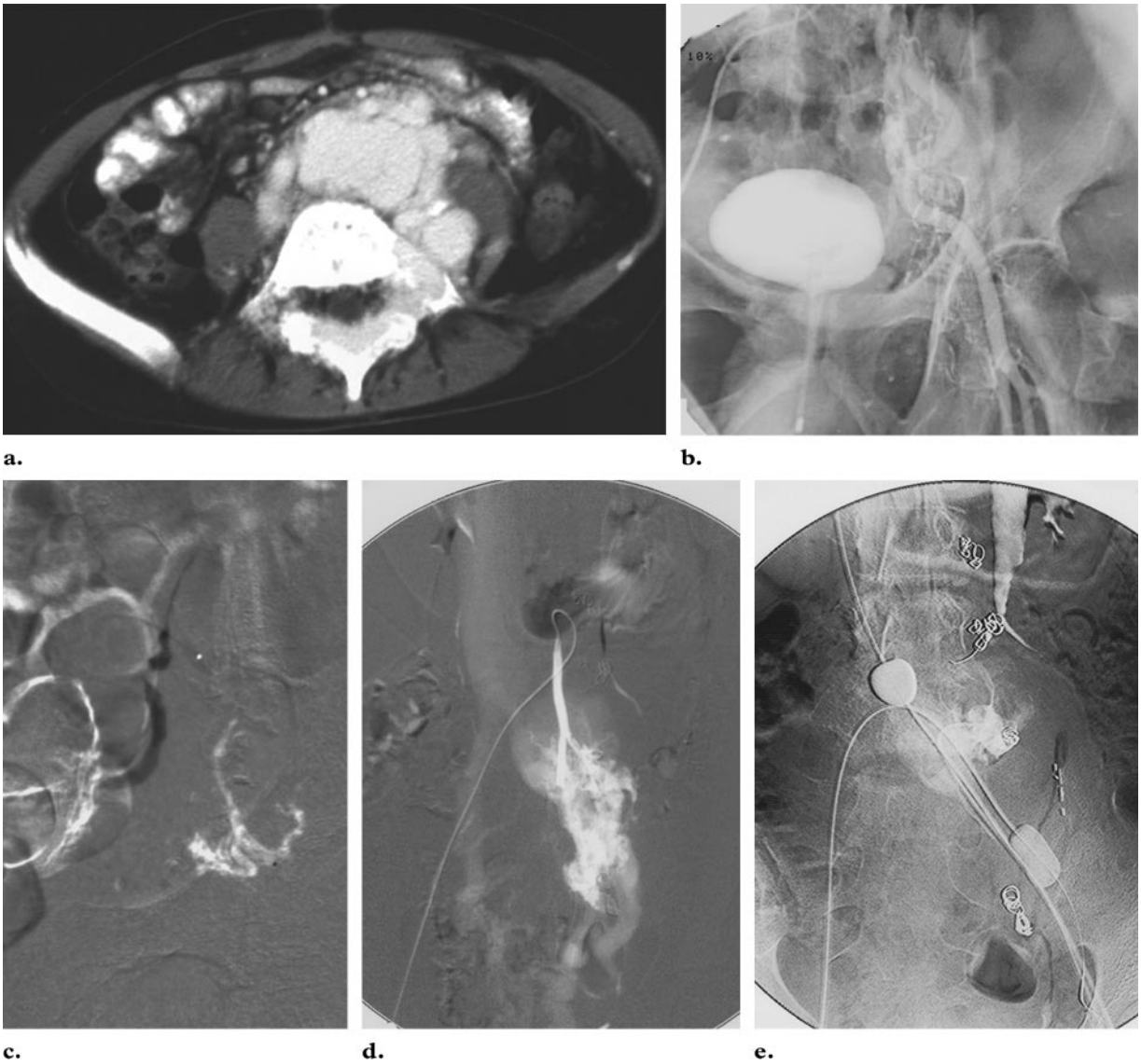
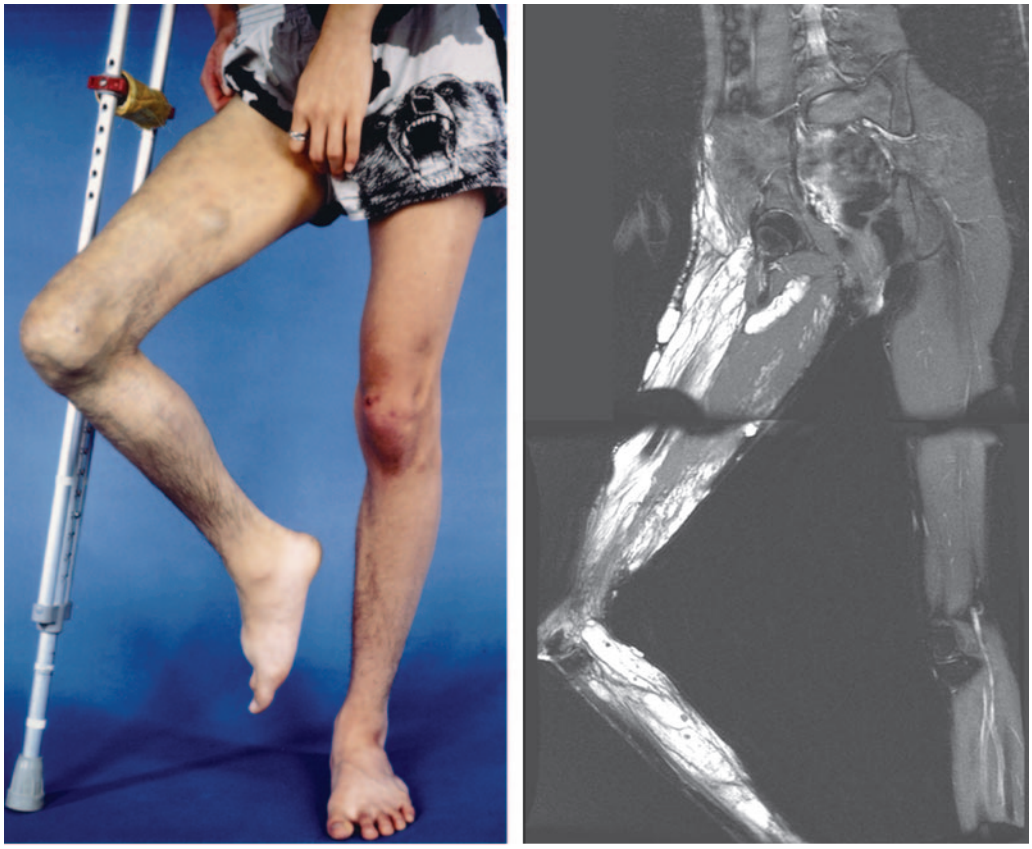


Figure 5. High-flow vascular malformation in the pelvis of a 14-year-old girl with general fatigue. **(a)** Axial contrast-enhanced CT scan shows dilated veins surrounding the abdominal aorta and extension of the veins to the prevertebral canal. **(b, c)** Preoperative angiograms obtained after fibered microcoils and *n*-butyl cyanoacrylate embolization were used to decrease the inflow before surgical exclusion. **(d)** Angiogram obtained after unsuccessful surgical ligation shows new feeding arteries formed from the superior and inferior mesenteric arteries. Although 20-mm occlusive balloon catheters were placed in the drainage vein, blood flow stasis was not achieved, and sclerotic agents such as ethanolamine oleate or polidocanol could not be used. **(e)** Angiogram obtained after additional *n*-butyl cyanoacrylate and coil embolizations were performed for palliation.

Destruction and deformation of local tissues are frequently seen, as well as a high rate of recurrence (Figs 5–7). High-flow lesions pose the greatest risk of all vascular malformations for severe bleeding or exsanguination. Even if the initial reduction in the volume of blood flow in the vascular malformation is acceptable, the rate of recurrence is high, and the volume of the recurrent lesion usually equals or exceeds the pretreatment volume within a short time. A multidisciplinary approach to treatment of this type of lesion is strongly recommended.

Teaching Point

Figure 6. Klippel-Trénaunay-Weber disease in a 16-year-old boy with swelling of the leg. Klippel-Trénaunay-Weber disease is characterized by venous angioma or combined capillary-venous-lymphatic malformation with bone and soft-tissue hypertrophy. **(a)** Photograph shows a dilated, blue vein that protrudes from the right leg. **(b)** Sagittal fat-saturated T2-weighted MR image shows the dilated vessel cavity with high signal intensity. Small areas of low signal intensity at the calf indicate phleboliths (or calcification). Sclerotherapy was not attempted in this case because of advanced muscular atrophy, which greatly increased the risk of adverse effects, such as skin ulcers or neurologic deficit.



a. b.

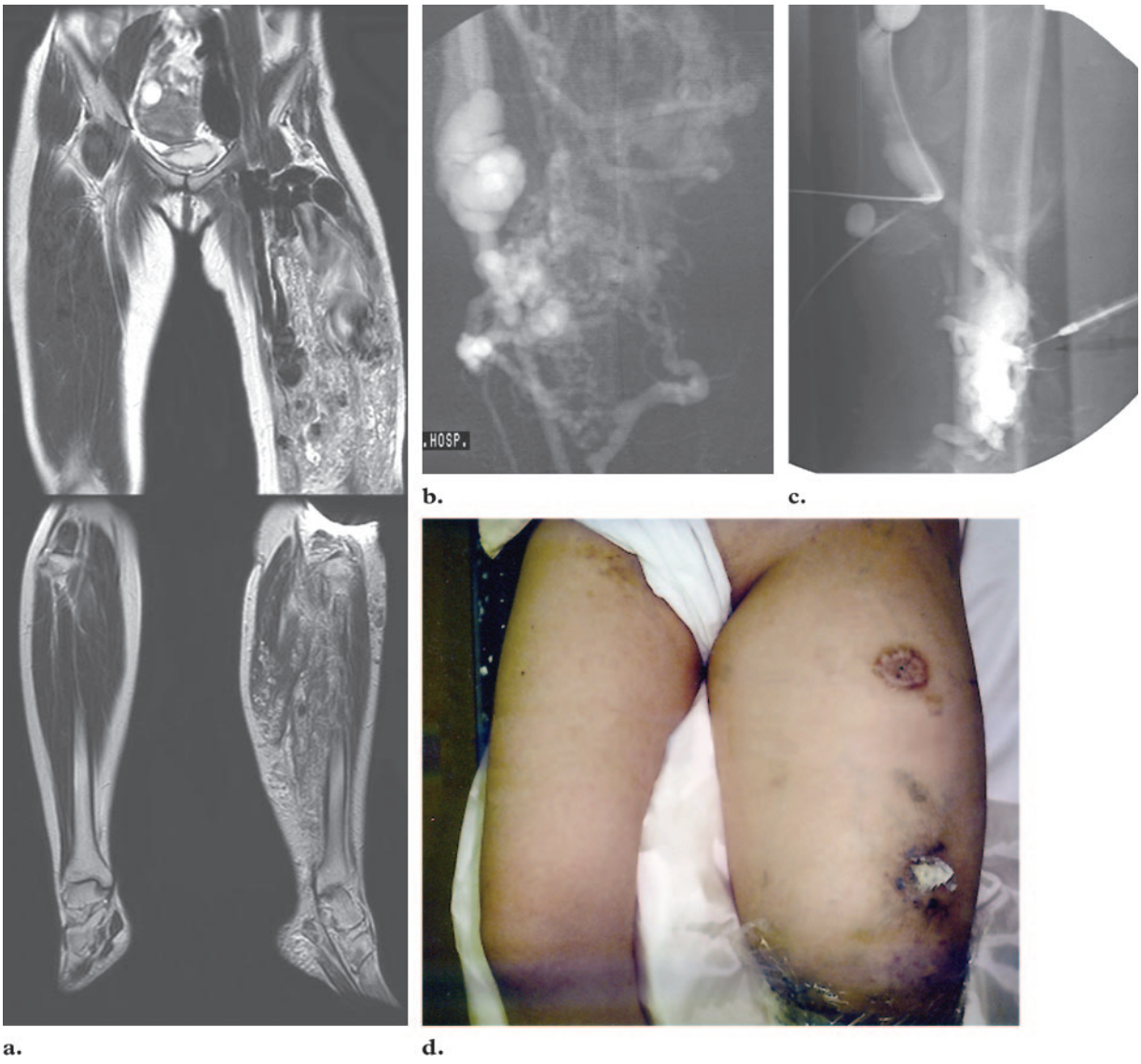
Follow-up

After the procedure, distal blood flow and nerve sensation should be monitored. A narcotic or nonnarcotic anti-inflammatory drug is generally used to relieve severe pain. After the postsclerotic period (about 3 days), CT with contrast material enhancement, MR imaging, or color Doppler US can be used to evaluate the efficacy of therapy (28), and phlebography is not necessary. During the follow-up period, the nidus may decrease in volume and signal intensity on T2-weighted MR images.

Patients' symptoms should also be carefully monitored during the follow-up period. After the procedure, patients complain of swelling and discomfort in the area of the treated lesion. Usually, these sensations decrease day by day, and a single administration of a nonnarcotic anti-inflammatory drug is sufficient. At least 2 years of follow-up is recommended to detect any recurrence and determine whether complications have worsened (or resolved).

Finally, we must emphasize that the percutaneous treatment of disabling vascular malformations requires the expertise of interventional radiologists who are familiar with the characteristics of these lesions and who are personally experienced with all currently acceptable types of therapy. They must be especially cognizant of the potential severe complications that can ensue during or following these interventions. They must also be able to follow up these patients over the long term to treat recurrences. These patients should ideally be referred to a multidisciplinary vascular clinic that specializes in the management of these complex lesions.

Figure 7. Parks-Weber syndrome in a 21-year-old woman with cardiac failure. Parks-Weber syndrome is characterized by vascular malformation with an arteriovenous fistula. **(a)** Coronal T2-weighted MR image shows multiple flow voids throughout the entire left leg. **(b)** Angiogram shows chaotic vascular loops and multiple arteriovenous fistulas. **(c)** Image obtained during phlebography after percutaneous absolute ethanol sclerotherapy, ethanolamine oleate sclerotherapy with balloon occlusion at the drainage vein, coil embolization, and stent-grafts were used to improve clinical symptoms. Skin ulcers were observed near the absolute ethanol injection area. **(d)** Photograph shows broad skin ulcers caused by increased venous pressure in the gastrocnemius area after the procedures.



Summary

Vascular malformations represent some of the most difficult challenges in the field of interventional radiology. To assess the extent of vascular malformations and flow velocity, CT, Doppler US, and MR imaging are useful. Phlebography and angiography are useful to confirm the diagnosis and evaluate the extent of the lesion. Conservative treatment is recommended in most cases, especially for patients with tolerable symptoms. The best way to manage patients with such malformations is to treat them on a regular basis. A dedicated team approach by surgeons, internal medicine specialists, interventional radiologists, and psychiatrists is necessary for appropriate management.

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