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Venous malformations

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ABSTRACT

Venous malformations are slow-flow congenital malformations. They consist of abnormal venous channels that do not involute. Venous malformations can either be superficial or involve deeper structures. Patients with venous malformations are often symptomatic. The most common complaint is pain from congestion, mass effect, or compression of neural structures. Swelling, compromise of function, and disfigurement are other common symptoms. Large lesions cause coagulopathy. Therapeutic options for the treatment of these patients include sclerotherapy, compression garments, and surgical resection. These complex patients are best treated in a multi-disciplinary clinic environment, as they require long-term follow-up throughout childhood into adulthood.

Introduction

Congenital venous malformations (VMs) are a common vascular malformation and consist of abnormal veins that can be localized or diffuse. The incidence is approximately 1–2/10,000 patients.[1] VMs are composed of mitotically inactive endothelium with scant mural smooth muscle.[2] They lack valves or direct large communication with the arterial system. Communication to the venous system is present via variably sized, though sometimes imperceptible, vessels.[3] VMs can be superficial within the dermis and subcutaneous tissues or deeper and infiltrate muscle or bone. VMs can be discreet entities or may be infiltrative and invade multiple tissue planes. They can also be present throughout the body as well as in visceral locations and can occur in isolation or in conjunction with other malformations.

VMs are present, if not always apparent, at birth. Superficial lesions have a bluish compressible mass that characteristically enlarges in a dependent position. In infants, positional volume changes can help distinguish the VM from a deep hemangioma. Deeper VMs may not be as apparent at birth but will often become symptomatic, particularly when they reside within the muscle or joint compartments. These are considered slow-flow malformations. They grow generally in proportion to the child and do not involute. Venous malformations can be present throughout the body and can also be found in combination with other vascular malformations, including most commonly lymphatic malformations, but also are seen with capillary malformations and occasionally with arteriovenous malformations.

The VM is thought to be a localized developmental defect of the vasculature characterized by enlarged endothelial cell venous channels surrounded by sparsely distributed vascular smooth muscle.[4,5] Most VMs occur sporadically. However, there are descriptions of families with venous malformations in many generations. These inherited VMs are often more numerous and are attributed to germ line mutations in the endothelial cell tyrosine kinase receptor TIE-2. The TIE-2 signaling pathway is essential for communication of endothelial cell smooth muscle during development of the venous system, with the activation of the angiopoietin family.[6] Mutations in the TIE-2 gene on the long arm of chromosome 9 is consistent with the familial type of VM and have also been found on about 50% of sporadic VMs.[7]

The most common symptom ascribed to VMs is pain. Pain can be due to several factors including (1) local compression of adjacent structures including muscles, joint, and nerves; (2) congestion and thrombosis due to venous stasis within the malformation, sometimes causing phleboliths (small calcific thrombi); and (3) hemorrhage into surrounding tissues and joints.[8] Venous malformations may also enlarge and become symptomatic with trauma, puberty, or during pregnancy. Without treatment over time, VM will generally undergo expansion.

Coagulation abnormalities are common with VM. Many patients develop pain secondary to the development of a localized intravascular coagulopathy (LIC)[9] due to stasis and abnormal venous endothelium. Abnormalities in the coagulation profile are common and are often proportional to the size of the VM. Many patients with extensive venous malformations have been found to have elevated D-dimer levels. D-dimer is a sensitive marker for

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thrombus formation and fibrinolysis and can be used as a negative predictive marker when trying to exclude the diagnosis of a VM. LIC is characterized by an increase in D-dimer level, normal platelet count, and decreased fibrinogen level. Patients with extensive LIC are at risk of systemic thromboembolism particularly with intervention and should be monitored carefully. Many patients may benefit from the use of low-molecular-weight heparin particularly during times of increased risk such as long travel, bed rest, pregnancy, and during or after surgical or interventional procedures.

When considering therapeutic options for VM, understanding the extent of disease can facilitate tailoring management strategies. Doppler ultrasonography, MRI, and direct-puncture venography can be performed to assess the extent of the lesion. These patients should be screened with a basic coagulation profile including complete blood count, prothrombin time (PT), partial thromboplastin time (PTT), D-dimer, and fibrinogen. More extensive clotting profiles, including testing for factor V Leiden, plasminogen activator inhibitors, and methylenetetrahydrofolate reductase, can also be performed if the initial screen is positive.

Types

Sporadic venous malformation

Sporadic venous malformations are the most common of venous malformations and account for approximately 94% of venous malformations.[3] These malformations can vary in size and shape, can be localized or diffuse and infiltrative, and can be superficial or involve deep structures including muscle, bone, and visceral organs. They are typically seen in the head and neck (40%), extremity (40%), and trunk (20%).[8,10,11]

Glomuvenous malformation

The most common familial form of venous anomaly is multiple glomuvenous malformation (formerly referred to as glomangioma) that account for about 5% of all venous malformation.[3] These are bluish raised nodules often found on the extremities which tend to involve the skin and subcutaneous tissues. Vikkula et al. have demonstrated mutation of the glomulin gene on chromosome 1 to be causal for this disorder.[12] Glomuvenous lesions can be clinically differentiated from the more commonly seen venous malformations. They appear as raised, bluish-purple lesions with a cobblestone surface and are often painful on palpation. Biopsy is generally not necessary, but histology reveals scattered glomus cells and a variable abundance of smooth muscle cells. Symptomatic lesions are best managed by complete surgical excision if possible. Unfortunately, they are often widespread and not easily amenable to excision. Painful areas can be treated with sclerotherapy, although this modality is not as efficacious as in common sporadic lesions. Sclerotherapy will not improve the purple coloration.

Blue rubber bleb nevus syndrome

Blue rubber bleb nevus syndrome or multiple venous malformations were first described by Gascoyen in 1860 and further characterized by William Bean in 1958, and given the eponym Bean syndrome.[13] This syndrome is characterized by discrete venous malformations of varying size usually between 1 and 2 cm in size. Lesions most frequently occur on the skin and within the gastrointestinal (GI) tract. They are typically present on the plantar and palmar surfaces. The morbidity and mortality associated with this syndrome depend on the extent of visceral organ involvement. Lesions within the GI tract may be associated with significant bleeding. These patients do not have large-volume spontaneous hemorrhage but rather more indolent bleeding whereby they develop chronic anemia requiring ongoing transfusions and iron replacement. These are generally addressed with surgical resection of lesions within the GI tract. This condition is discussed in more detail in the Visceral Vascular Malformation article in this edition.

Imaging

The imaging of venous malformations is mainly performed with Doppler ultrasonography (US) and magnetic resonance imaging (MRI). Conventional radiographs, while often unnecessary, may show phleboliths. Phlebotliths are nearly pathognomic for venous malformations; however, they are only present in up to 30% of radiographs.[10] US is typically the first step in the imaging evaluation due to availability, feasibility, lack of ionizing radiation, and the only rare requirement for sedation in children. The US appearance of venous malformations is variable depending on the location and type of venous malformation. Appearance can range from a focally dilated vein (similar to adult varicosities) to the more commonly encountered fluid-filled cavitary lesion with septations (Fig. 1).[3,10,14,15] Presence of echogenic debris or shadowing phleboliths is highly specific for the diagnosis of venous malformation.[3] The cystic spaces are compressible on real-time US imaging and show little to no flow on Doppler interrogation. Valsalva maneuvers and compression may demonstrate increased Doppler flow. Arterial flow may be seen within and around the VM from adjacent arteries.[3,10] US is limited in its ability to evaluate extensive and deep lesions.

MRI best demonstrates VMs and their extent and relationship to adjacent structures. In general, VMs show an increased signal on T2 sequences in a lobular or serpiginous pattern (Fig. 2).[3,10,14,15] Decreased T2 signal can be seen within areas of thrombosis

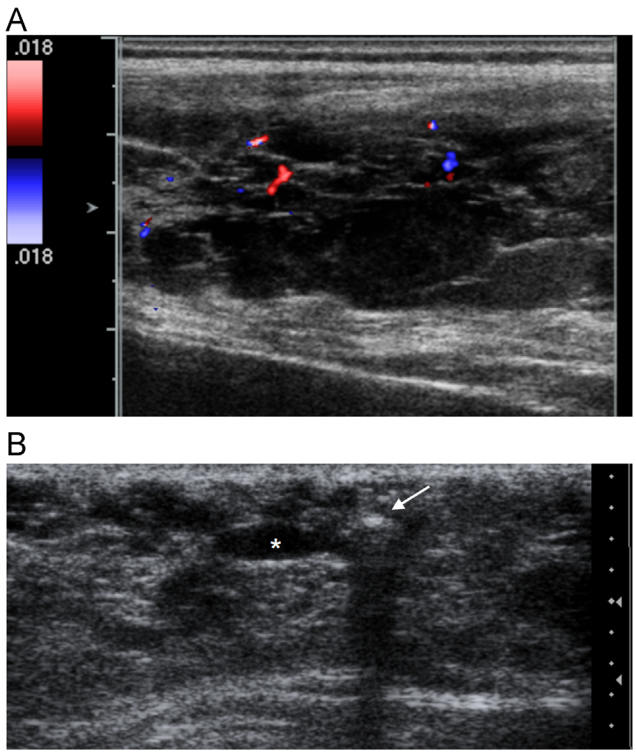

Fig. 1. Ultrasound images showing echogenic debris and phleboliths. (Color version of figure is available online.)