Management of Venous Malformations

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KEYWORDS

• Glomuvenous • Sclerotherapy • Treatment
• Vascular anomaly • Vascular malformation
• Venous malformation • Verrucous hemangioma

CLINICAL FEATURES

Venous malformation (VM) results from an error in vascular morphogenesis; veins are dilated with thin walls and abnormal smooth muscle.[1] Consequently, lesions expand, flow stagnates, and clotting occurs. Although a VM is present at birth, it may not become evident until childhood or adolescence when it has grown large enough to cause a visible deformity or symptoms. Lesions are blue, soft, and compressible; hard calcified phleboliths may be palpable. VMs may range from small localized skin lesions to diffuse malformations involving multiple tissue planes and vital structures.

VMs are typically sporadic and solitary in 90% of patients; 50% of patients have a somatic mutation in the endothelial receptor TIE2.[2,3] Angiopoietins, the ligands for TIE2, are involved in angiogenesis; the mutation uncouples endothelial cells and pericytes altering venous development.[3,4] Sporadic VMs are usually larger than 5 cm (56%); single (99%); and located on the head/neck (47%), extremities (40%), or trunk (13%).[2] Almost all lesions involve the skin, mucosa, or subcutaneous tissue; 50% of the lesions also affect deeper structures (ie, muscle, bone, joints, viscera).[2]

Approximately 10% of patients with VM have multifocal familial lesions, either glomuvenous malformation (GVM) (8.0%) or cutaneomucosal VM (CMVM) (2.0%).[2,5] GVM is an autosomal dominant condition with abnormal smooth muscle–like glomus cells along the ectatic veins and is caused by a loss-of-function mutation in the glomulin gene.[6,7] Lesions are typically multiple (70%), small (two-thirds are <5 cm), and located in the skin and subcutaneous tissue. GVM involves the extremities (76%), trunk (14%), or head/neck (10%). GVM is more painful than typical VM, especially on palpation.[7] It is reported that 17% of patients develop new lesions over time.[7] CMVMs are small multifocal mucocutaneous anomalies caused by a gain-of-function mutation in the TIE2 receptor.[4] The condition is autosomal dominant and less common than GVM. Lesions are small (76% of the lesions are <5 cm); multiple (73%); and located on the head/neck (50%), extremity (37%), or trunk (13%).[2] Unlike GVMs, CMVMs are not painful on palpation.[2] Cerebral cavernous malformation (CCM) is a rare familial disorder with VM involving the brain and spinal cord; patients may also have hyperkeratotic skin lesions.[5,8] The disorder results from mutations in CCM1/KRIT1, CCM2, and CCM3 genes, and patients are at risk for developing new intracranial malformations and hemorrhage.[9–11]

Blue rubber bleb nevus syndrome (BRBNS) is a rare condition with multiple small (<2 cm) VMs

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involving the skin, soft tissue, and gastrointestinal tract.[12–14] Morbidity is primarily associated with gastrointestinal bleeding requiring long-term blood transfusions. Diffuse phlebectasia of Bockenheimer is an eponym occasionally used for an extensive extremity VM involving the skin, subcutaneous tissue, muscle, and bone.[15] Sinus pericranii is a venous anomaly of the scalp or face with transcalvarial communication with the dural sinus. Verrucous hemangioma (VH) most closely resembles a hyperkeratotic VM (verrucous VM), although some histologic features are similar to an involuted infantile hemangioma.[16] Lesions range from 2 to 8 cm and are located on an extremity (91%) or the trunk (9%).[16] VH involves the skin and subcutis, becomes more hyperkeratotic over time, and is frequently associated with bleeding. VMs may also be a part of a combined malformation, particularly lymphatic, because lymphatics arise from veins embryologically.[1,17–19] Phlebectasia, a distinct venous anomaly, has 3 major forms: (1) sporadic (also called congenital varicosity), (2) associated with lymphatic malformation (LM), and (3) syndromic (eg, Klippel-Trénaunay syndrome).[20]

Complications of VMs depend on the extent and location of the anomaly. Lesions often cause psychosocial morbidity because of their appearance. Patients can have pain and swelling from dependent positioning or secondary to thrombosis and phlebolith formation. Head and neck VMs may present with mucosal bleeding or progressive distortion, leading to airway or orbital compromise. Extremity VMs can cause leg length discrepancy, hypoplasia due to disuse atrophy, pathologic fracture, hemarthrosis, and degenerative arthritis.[21] VMs of muscle may result in fibrosis and subsequent pain and disability.[22] Patients with phlebectasia, particularly when it communicates with the deep venous system through large perforators, are at risk for thrombosis and pulmonary embolism. Gastrointestinal VMs can cause bleeding and chronic anemia. Stagnation within a large VM results in a localized intravascular coagulopathy (LIC) and thromboses. A VM is especially problematic because it is progressive; it enlarges over time, particularly during adolescence; and often reexpands after treatment. Consequently, most patients who present with asymptomatic lesions will ultimately require intervention.

DIAGNOSIS

At least 90% of VMs are diagnosed by history and physical examination.[23,24] The primary differential diagnosis is LM. Patients should be queried about a family history of similar lesions, especially if GVM or CMVM is suspected. Unlike sporadic VMs, familial lesions are usually smaller, multiple, and superficial; GVM is painful on palpation. If the diagnosis is equivocal, a hand-held Doppler will rule out a fast-flow lesion and dependent positioning will cause a VM to enlarge.

Small superficial VMs do not require further diagnostic workup. However, large or deeper lesions are evaluated by magnetic resonance imaging (MRI) or ultrasonography (US) to (1) confirm the diagnosis, (2) define the extent of the malformation, and (3) plan treatment. To adequately assess a vascular anomaly, MRI sequences are obtained with fat suppression and contrast. VMs are hyperintense on T2-weighted images, except for phleboliths, which demonstrate a low-intensity signal on both T1- and T2-weighted sequences. Abnormal arterial flow is not present.[25] VMs can appear less intense after treatment because of scar tissue.[25] VMs enhance heterogeneously after gadolinium administration. Magnetic resonance venography delineates the deep venous system in extremity lesions. US is a good alternative for some localized VMs and does not require sedation in young children. US findings include compressible anechoic to hypoechoic spaces, with septations that show no flow on color Doppler and are separated by more solid regions of variable echogenicity.[26] Phleboliths are hyperechoic, with acoustic shadowing.[27] Computed tomography is occasionally indicated to assess an osseous VM. Intralesional venography is not usually needed for confirming the diagnosis but is essential before sclerosant injection. Phlebectasia is initially imaged with US to demonstrate the dilated incompetent veins and large perforators. Histopathologic diagnosis of VM is rarely necessary but may be indicated if findings of imaging are equivocal.

MANAGEMENT

Nonoperative

Patients with GVM or CMVM are counseled about the risk of developing new lesions as well as the autosomal dominant inheritance pattern. The natural history of VM is explained, including the possibility of expansion and phlebothrombosis. Because VMs are at a greatest risk for expansion in adolescence, sex hormones may be involved in its pathogenesis. Consequently, the authors recommend progesterone-only oral contraceptives for women with problematic lesions because estrogen has more potent proangiogenic activity than progesterone.[28–31] Patients with a large extremity VM are prescribed custom-fitted