Management of Venous Malformations

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KEYWORDS

• Venous malformation • Spongiform venous malformation • Phlebectatic venous malformation
• Slow-flow vascular malformation • Glomuvenous malformation • Fibroadipose vascular anomaly
• Verrucous venous malformation • Bockenheimer disease

KEY POINTS

- An overview of all the different types of venous malformations (VMs).
- A comprehensive guide on diagnosing VMs, outlining the necessary work-up and distinguishing between various subtypes.
- A comprehensive overview of the therapeutic modalities, and their combinations, available for various VM subtypes, along with guidance on selecting the most appropriate treatment based on the affected tissues.

PATHOPHYSIOLOGY AND CLASSIFICATION

Venous malformations (VMs) are among the most frequently encountered vascular anomalies in plastic and reconstructive surgery clinics, particularly within specialized multidisciplinary referral centers. Their prevalence is estimated at approximately 1 per 2000 to 5000 individuals.[1] VMs originate from aberrant development of the venous system, resulting in enlarged, structurally immature venous channels with a paucity or absence of smooth muscle within the vessel wall. These lesions are classified as slow-flow malformations following the ISSVA classification,[2] characterized by venous stasis and progressive distension over time. They are caused by a hyperactivation of the TIE2-PI3K-AKT-mTOR pathway. Most lesions occur sporadically whereas hereditary multifocal lesions represent about 6% of patients (**Table 1**).[3] Their management varies according to subtypes and involved tissues, and the VASCERN-VASCA generated a patient pathway to help guide this process.[4]

Isolated

Venous malformation

VMs are composed of abnormally formed, dilated, and ectatic veins with slow blood flow. Congenital, but not always visible at birth, they typically grow proportionally with the child. These malformations are distinct from varicose veins and are composed of thin-walled venous channels that lack normal smooth muscle, leading to their distensibility and risk of thrombosis.[5] They can either be spongiform (**Fig. 1**A, B), which are the most frequent, or phlebectatic (**Fig. 2**A, B), according to venous morphology[2] and can appear anywhere on the body. The lesion can be well localized or diffusely

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Abbreviations

BEST	bleomycin electrosclerotherapy
BRBNS	blue rubber bleb naevus syndrome
CCM	cerebral cavernous malformation
CLOVES	congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and skeletal anomalies or scoliosis
CM	capillary malformation
DIC	disseminated intravascular coagulopathy
FAVA	fibro-adipose vascular anomaly
GoF	gain-of-function
GVM	glomuvenous malformation
HCCVM	hyperkeratotic cutaneous capillary venous malformation
LMWH	low molecular weight heparin
MSVM	multiple sporadic venous malformation
PHTS	*PTEN*-associated hamartoma tumor syndrome
PROS	*PIK3CA*-related overgrowth spectrum
QoL	quality-of-life
VM	venous malformation
VMCM	multiple cutaneous and mucosal venous malformation
VMOS	vascular malformation–osteolytic subtype
VVM	verrucous venous malformation

infiltrating. It is estimated that approximately half of VMs harbor a sporadic gain-of-function (GoF) TEK mutation[6] and about 20% are caused by sporadic GoF *PIK3CA* mutations.[7]

Verrucous venous malformation

Verrucous venous malformation (VVM) comprises aberrant clusters of malformed dermal venule-like channels underlying hyperkeratotic skin (**Fig. 3**).[8] They typically present as raised, reddish-purple, hyperkeratotic lesions that extend into the subcutis. Most lesions occur in an extremity (usually legs) sometimes extending to the trunk. Hyperkeratosis increases over time, resulting in the typical verrucous appearance frequently associated with scaling and crusting.[9,10] VVM can rarely present as a purely subcutaneous lesion[11] and are caused by GoF mutations in *MAP3K3*.[8]

Fibroadipose vascular anomaly

Fibro-adipose vascular anomaly (FAVA) is composed of an adipose component and a VM component. They usually present in the extremities and are characterized by a unique intramuscular lesion that can sometimes extend, into adjacent tissues (**Fig. 4**A–D).[12,13] Almost all patients present with pain and functional impairment as part of their symptoms. FAVA seems to be caused by *PIK3CA* mutations.[14]

Bockenheimer disease

Bockenheimer disease refers to an extensive form of VM characterized by longitudinal involvement of a limb, with infiltration across multiple anatomic layers, including the skin, subcutaneous tissue, muscles, and skeletal structures. This entity follows a progressive course and is associated with substantial clinical burden, manifesting as chronic pain, limb enlargement, cutaneous color changes, and progressive functional impairment. It is associated with thrombotic events and frequent intra-articular involvement.[15,16] Bockenheimer disease is caused by mutations in the *TEK* gene.[16]

Multifocal

Most VM will present as a solitary sporadic lesion. Less frequently, VM can be multifocal and some multifocal VMs can be hereditary (**Fig. 5**, green box: Multiple VMs). In the presence of multifocal VMs, hereditary diseases should be excluded and genetic counseling sought when clinically indicated.[17]

Sporadic multifocal venous malformations

Multiple sporadic VMs (MSVM) constitute a nonhereditary, multifocal VM phenotype (**Fig. 6**). Clinically, MSVM closely resemble VMs of the cutaneous-mucosal type (VMCM, see below) but occur in the absence of a familial history. They typically manifest as numerous small lesions, generally measuring less than 5 cm, with a raised contour and variable bluish discoloration, affecting the skin and oral mucosa and, less commonly, deeper structures such as subcutaneous tissue or skeletal muscle. Lesions most often involve the cervicofacial region and the extremities, display a dome-shaped configuration, have a soft consistency on palpation, and show limited compressibility. Owing to their restricted size, these lesions are usually clinically silent.[18,19] MSVM are caused by GoF *TEK* mutations.[18]

Blue rubber bleb naevus syndrome (BRBNS), or Bean syndrome, is typically characterized by the presence at birth of a prominent lesion often referred to as a dominant malformation, followed by the progressive appearance of multiple VMs involving the skin and internal organs. These lesions show a particular predilection for the palms and soles and are notable for their soft, rubber-like texture, frequently associated with surface hyperkeratosis. Visceral involvement most commonly affects the gastrointestinal tract, where VMs may lead to chronic bleeding, iron-deficiency anemia, and mechanical complications such as volvulus

Table 1
Summary of the different venous malformation subtypes with the underlying causative genetic mutation and available treatment options

Subtype	Characteristics	Gene	Treatment Options
Sporadic spongiform VM	• Bluish color • Compressible • Possible LIC	50% *TEK* 20% *PIK3CA*	Sclerotherapy Surgery Targeted medical therapy nd:YAG BEST
Sporadic phlebectatic VM	• Risk of pulmonary embolism if direct connections with deep veins • No LIC	50% *TEK* 20% *PIK3CA*	Endovenous laser therapy Sclerotherapy Targeted medical therapy
VVM	• Hyperkeratotic skin • No LIC	*MAP3K3*	Surgery nd:YAG Targeted medical therapy
FAVA	• Intramuscular • VM and adipose component • No LIC	*PIK3CA*	Surgery Cryotherapy
Bockenheimer disease	• Diffuse VMs • Mainly lower limbs • Frequent intra-articular component • LIC	*TEK*	Targeted medical therapy Sclerotherapy BEST Surgery
MSVM	• Usually multiple small lesions • New lesions may appear • LIC	*TEK*	Sclerotherapy Surgery nd:YAG Targeted medical therapy
BRBNS	• One larger lesion at birth • Multiple smaller lesions • Palm and sole • Digestive tract lesions • New lesions may appear • LIC	*TEK*	Sclerotherapy Surgery Targeted medical therapy BEST nd:YAG
VMCM	• Usually small lesions • New lesions may appear • Possible LIC	*TEK (hereditary)*	Sclerotherapy Surgery nd:YAG Targeted medical therapy
HCCVM	• Hyperkeratotic skin • Intracerebral lesions (CCM) • No LIC	*KRIT1 (hereditary)* *CCM2 (hereditary), less frequent* *PDCD10 (hereditary), less frequent*	Surgery nd:YAG Targeted medical therapy
GVM	• Multiple bluish nodules • Not compressible • Painful • No LIC	*GLMN (hereditary)*	Surgery nd:YAG
VMOS	• Intra-osseous lesions • Mainly mandibula and maxilla • No LIC	*ELMO2 (hereditary)*	Sclerotherapy Surgery
Maffucci syndrome	• Spindle cell hemangiomas • Enchondromas • Risk of malignancy • No LIC	*IDH1* *IDH2*	Surgery
PROS	• Can present with VMs • Overgrowth • Possible LIC	*PIK3CA*	Targeted medical therapy Surgery Sclerotherapy

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Table 1
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Subtype	Characteristics	Gene	Treatment Options
PHTS	• Can present with atypical VMs • Difficult to distinguish from FAVA • Risk of malignancy • No LIC	*PTEN (hereditary)*	Surgery

Abbreviations: BEST, bleomycin electrosclerotherapy; BRNS, blue rubber bleb naevus syndrome; CCM, cerebral cavernous malformation; FAVA, fibro-adipose vascular anomaly; GVM, glomuvenous malformations; HCCVM, hyperkeratotic cutaneous capillary-venous malformations; LIC, localized intravascular coagulopathy; MSVM, multiple sporadic venous malformations; PHTS, *PTEN*-associated hamartoma tumor syndrome; PROS, *PIK3CA*-related overgrowth spectrum; VM, venous malformation; VMOS, vascular malformation–osteolytic subtype; VMCM, multiple cutaneous and mucosal venous malformation; VVM, verrucous venous malformation.

or intestinal ischemia. The presence of gastrointestinal VMs is regarded as a defining and pathognomonic feature of BRBNS.[18,19] BRBNS is caused by GoF *TEK* mutations.[18]

Hereditary multifocal venous malformations

Multiple cutaneous and mucosal VMs (VMCM) are classically characterized by the presence of numerous, small, multifocal VMs involving the skin and/or oro-mucosal surfaces, exhibiting a bluish discoloration. Very small, millimetric lesions are most often asymptomatic, although they may be of cosmetic concern, and they rarely ulcerate or bleed. Larger lesions, occasionally reaching several centimeters, may extend into subcutaneous tissues or underlying muscle and can be associated with pain. Considerable variability exists in lesion size, number, and distribution, both within and between affected families. VMCM may occur at any anatomic site and frequently involve the oral mucosa; more rarely, lesions may affect the gastrointestinal tract or anal mucosa.[19–21] VMCM is caused by *TEK* mutations.[18]

Hyperkeratotic cutaneous capillary VMs (HCCVMs) are hereditary VMs with a capillary malformation (CM) component associated with hyperkeratotic skin. Usually difficult to differentiate clinically from VVM (**Fig. 7**), they are associated with cerebral CMs, part of a larger spectrum of intracranial slow-flow vascular lesions referred to as cerebral cavernous malformations (CCMs).[22] HCCVM are more frequently seen in CCM1 but can be associated with CCM2 or 3. CCMs are inherited diseases caused by hereditary LoF mutation in *KRIT1*, *CCM2*, or *PDCD10*, respectively.[23]

Glomuvenous malformations (GVMs) are cutaneous venous anomalies histologically distinguished from VMs. They present as dilated venous channels containing characteristic glomus cells within their walls. Clinically, GVMs typically present as raised, nodular, and often multifocal lesions with frequent hyperkeratosis, producing a cobblestone-like surface appearance (**Fig. 8**A–C). Lesions display variable coloration, ranging from pink to deep violaceous or dark blue, and most commonly involve the extremities, affecting the skin and subcutaneous tissues. In contrast to common VMs, GVMs are noncompressible and cannot be completely emptied with external pressure. Pain is a hallmark feature and is usually provoked by direct compression, whereas pain associated with other VMs more commonly occurs at rest, after

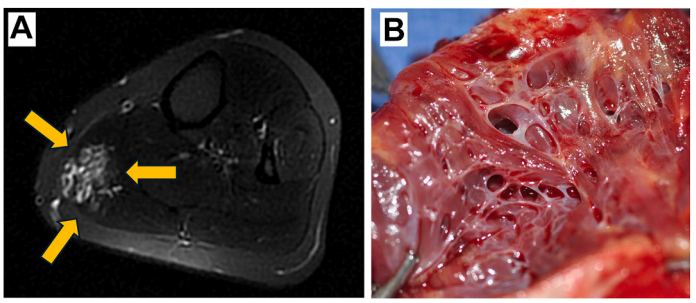

Fig. 1. (*A*, *B*) (*A*) T2-weighted MRI of a spongiform venous malformation (VM; *orange arrows*). (*B*) Per-operative view of a spongiform VM.

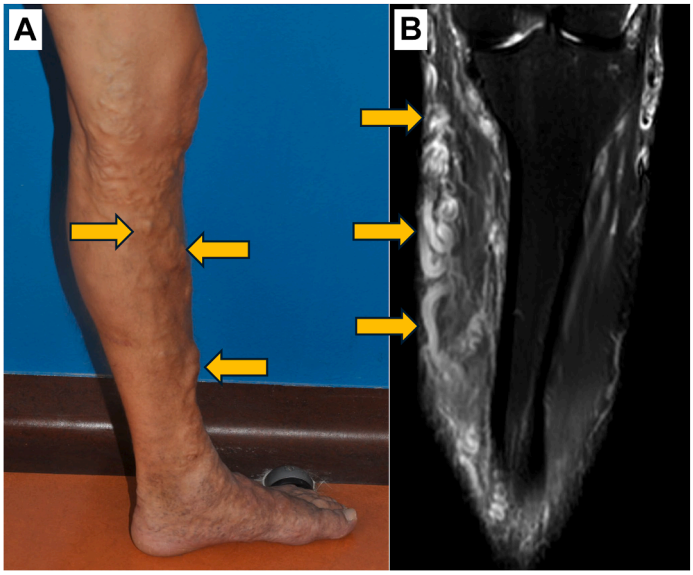

Fig. 2. (*A, B*) (*A*) Male patient with diffuse phlebectatic VM of left leg with an ectatic vein component (*orange arrows*). (*B*) T2-weighted MRI of the affected leg with subcutaneous tortuous and dilated veins (*orange arrows*).

physical activity, or in relation to hormonal changes.[24,25] GVMs are caused by hereditary LoF mutations in the glomulin gene (*GLMN*).[25]

Vascular malformation–osteolytic subtype (VMOS) is an exceptionally rare autosomal recessive disorder characterized by aberrant vascular development within bone, leading to progressive osteolysis. The condition predominantly affects intramembranous bones, with a marked predilection for the mandible and maxilla. Clinically, patients often present with progressive jaw swelling and mandibular enlargement, accompanied by gingival hypertrophy and recurrent spontaneous intraoral bleeding. Dental manifestations are common and include enamel hypoplasia, delayed tooth eruption, and an increased susceptibility to caries.[26,27] VMOS are caused by hereditary LoF mutations in *ELMO2*.[26]

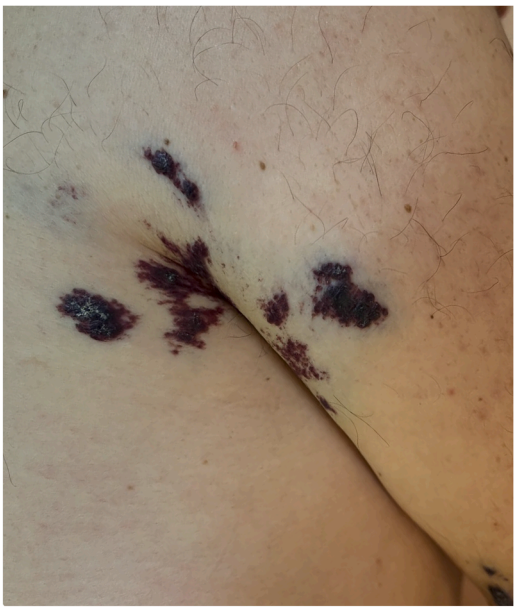

Fig. 3. Verrucous venous malformation of the right axilla and posterior arm. Notice the darker color than spongiform VMs and the hyperkeratotic skin.

Syndromic

VMs can be associated with other clinical manifestation as part of syndromes, either sporadic or hereditary (see **Fig. 5**, light brown box: Syndromic VM). In Maffucci syndrome, patients present with multiple small VMs, that histologically are composed of spindle cells and are called spindle cell hemangiomas. Patients also present with multiple enchondromas.[28] Maffucci syndrome is not hereditary but associated with an increased risk of malignancy[4] and caused by mutation in *IDH1* or *IDH2*.[28]

PIK3CA-related overgrowth spectrum (PROS) disorders encompass a heterogeneous group of conditions defined by the association of somatic *PIK3CA* variants with variable combinations of segmental overgrowth, slow-flow vascular anomalies, and epidermal nevi. Within this spectrum, CLOVES syndrome, an acronym for congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and skeletal anomalies or scoliosis, is a rare, multisystem disorder characterized by asymmetric overgrowth affecting adipose tissue, muscle, bone, and visceral structures. CLOVES patients can present with VMs. Klippel–Trenaunay

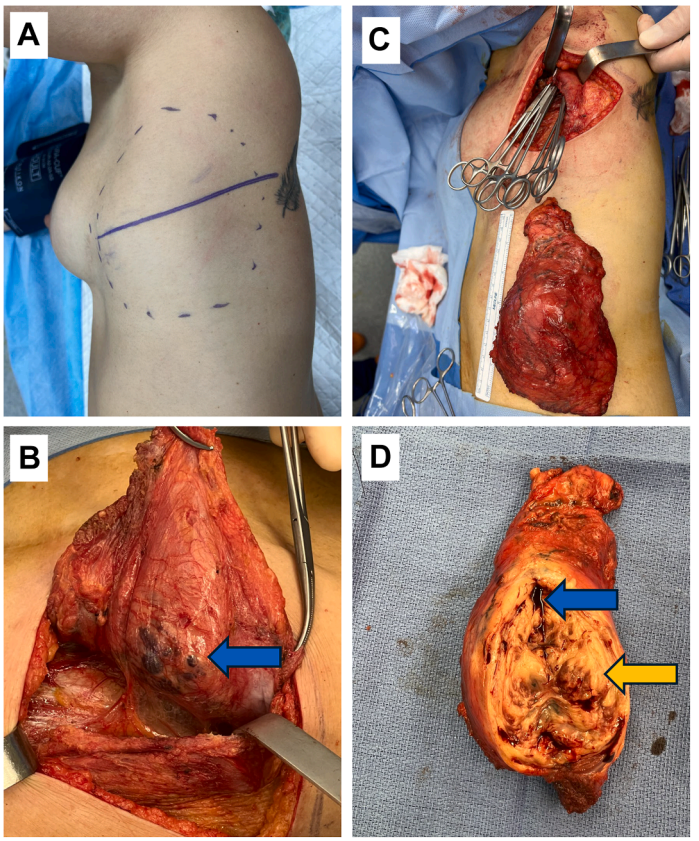

Fig. 4. (*A–D*) (*A*) Preoperative drawing of the incision line (*continuous line*) to resect a FAVA inside the left latissimus dorsi muscle (*dotted line*). (*B*) Caudal incision of the latissimus dorsi muscle which is elevated showing his deep surface with the visible VM component (*blue arrow*). (*C*) Partial resection of the latissimus dorsi muscle. (*D*) Incision of the FAVA showing the mixed venous component (*blue arrow*) and fat component (*orange arrow*).

syndrome represents a usually more localized PROS phenotype, typically involving a lower limb and pelvis, and is characterized by extensive CMs, frequently associated lymphatic anomalies, VMs, and progressive hypertrophy of soft tissues and bone. PROS are nonhereditary syndromes.[29]

PTEN-associated hamartoma tumor syndrome (PHTS) is a hereditary condition that can manifest as hamartomas with a vascular component, often exhibiting a fast-flow component. However, distinguishing fibroadipose lesions with a vascular component that present very subtle fast-flow characteristics from FAVAs can be challenging. PHTS is a hereditary condition caused by mutations in *PTEN* and associated with an increased risk of malignancy.[30]

CLINICAL PRESENTATION AND NATURAL HISTORY

Clinical presentation varies according to the type of VM and the tissues involved. VMs affecting the skin and/or superficial subcutis will present as a compressible lesion with a bluish color (**Fig. 9**). VVM/HCCVM will present with hyperkeratosis and GVM as bluish incompressible nodules. Without skin involvement, VM can present as a compressible swelling or mass, as opposed to FAVA which will not be compressible. Less frequently, VVM or GVM can present as strictly subcutaneous lesions.[11,25] Compression is not painful, except for GVMs or in case of local thrombosis. VMs can be painful, either caused by the lesion's volume, intravascular localized coagulopathy (LIC) or phleboliths that are calcified nodules resulting from chronic LIC. Phleboliths are pathognomonic of VMs and not encountered with VVM/HCCVM, GVM, or spindle cell hemangiomas.

VMs are congenital but mostly diagnosed during childhood and will grow proportionally with the child.[31] Volume or symptoms increase can be observed during puberty or pregnancy.

DIAGNOSTIC EVALUATION

Clinical Assessment

Initial clinical assessment will allow to evaluate patient's symptoms, which are key to discuss treatment. VMs are chronic diseases and treatments are not always curative. That is why the principal aim often is treating symptoms. As

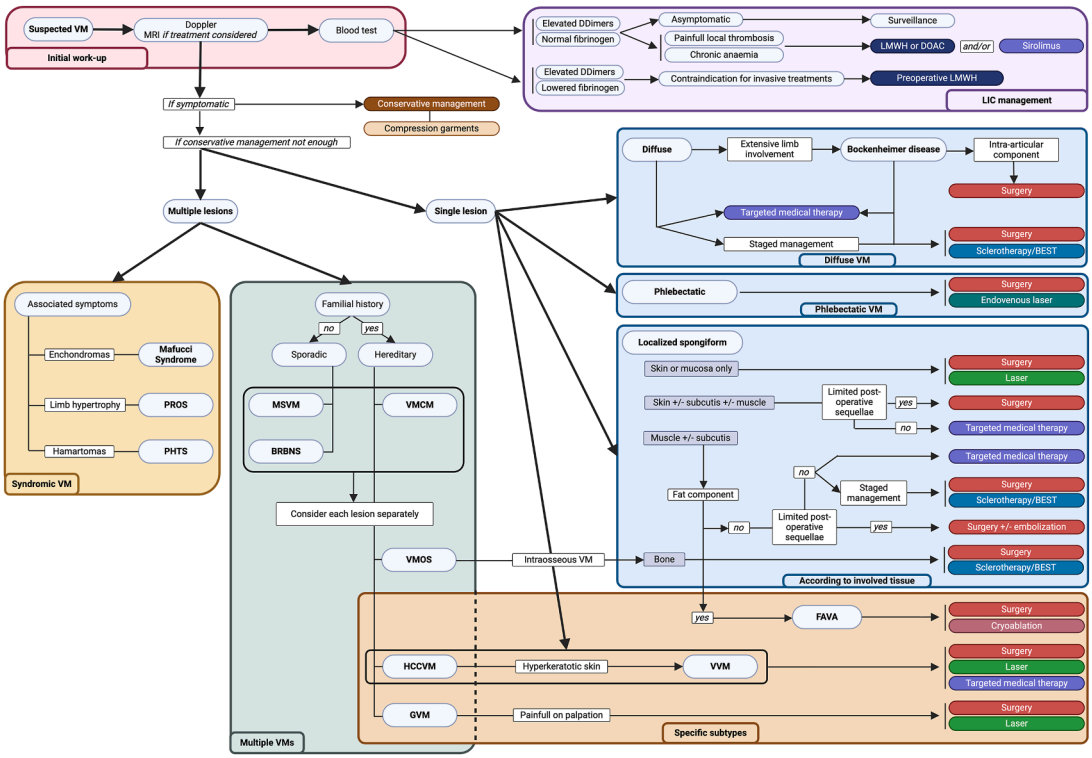

Fig. 5. Schematic representation of the different VM subtypes and their treatment options. BEST, bleomycin electrosclerotherapy; BRNS, blue rubber bleb naevus syndrome; DOAC, direct anticoagulants; FAVA, fibro-adipose vascular anomaly; GVM, glomuvenous malformations; HCCVM, hyperkeratotic cutaneous capillary-venous malformations; LIC, localized intravascular coagulopathy; LMWH, low molecular weight heparin; MSVM, multiple sporadic venous malformations; PHTS, *PTEN*-associated hamartoma tumor syndrome; PROS, *PIK3CA*-related overgrowth spectrum; VM, venous malformation; VMOS, vascular malformation–osteolytic subtype; VMCM, multiple cutaneous and mucosal venous malformation; VVM, verrucous venous malformation.

such, quality-of-life (QoL) is the main outcome that should be measured and followed. Specific QoL questionnaires have been developed specifically for vascular anomalies.[32,33]

Imaging Strategy

Ultrasound is usually the first examination to confirm slow flow inside the lesion. In 80% of cases, VMs appear as hypoechoic or heterogeneous and

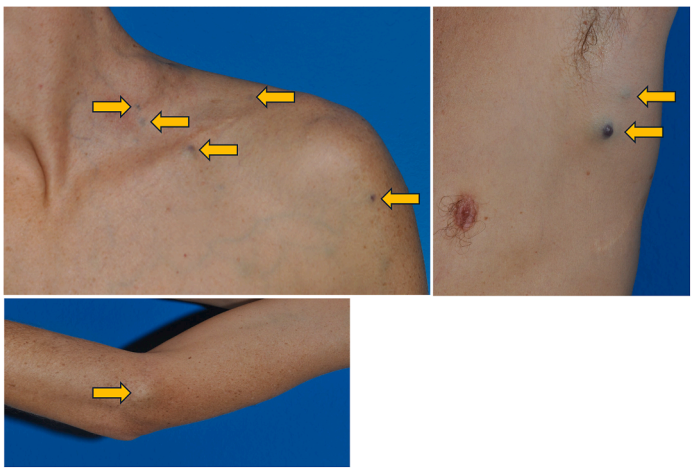

Fig. 6. Patient with MSVM presenting with multiple small subcutaneous VMs (*orange arrows*).

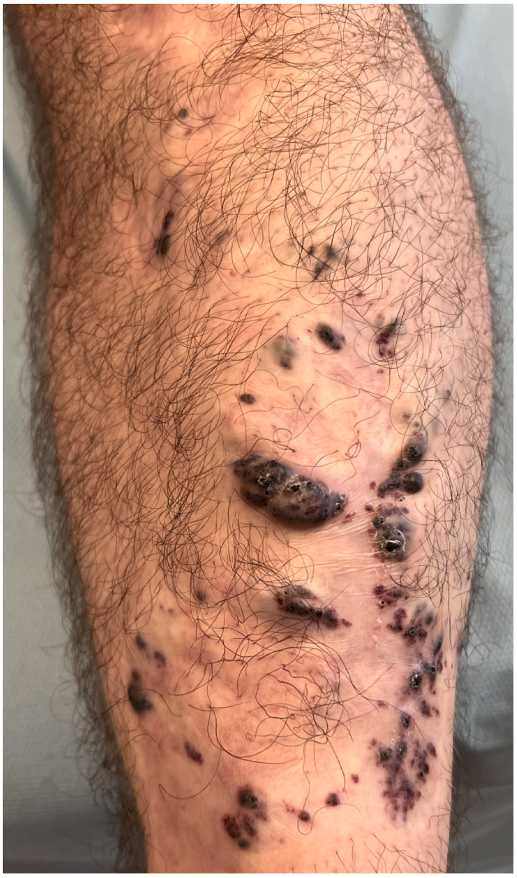

Fig. 7. Patient with HCCVM presenting multiple VMs involving the skin with a hyperkeratotic component.

compressible lesions.[4] The gold standard is an MRI with spin-echo T1 and fat saturated T2 weighted sequences before considering treatment. T1- and T2-weighted fat-saturated MRI images show how the vascular lesion relates to nearby organs, nerves, tendons, and muscles (see **Fig. 5**, red box: Initial work-up).

MRI angiography provides limited additional information; however, it can assist in excluding arteriovenous malformations. It is important to note that large vascular malformations may contain small feeding vessels, leading to a capillary blush which should not be misinterpreted as an arteriovenous malformation.[4]

Localized Intravascular Coagulopathy

VMs often lead to chronic consumptive coagulopathy, also referred to as LIC, which is characterized by significantly raised D-dimer levels even in otherwise healthy individuals (see **Fig. 5**, purple box: LIC management). Half of patients with VMs present with elevated D-dimers, which is even more frequent in multifocal VMs.[4] While generally manageable in daily life, this condition can escalate to disseminated intravascular coagulopathy (DIC) during surgical interventions. Clinical management typically involves monitoring D-dimer and fibrinogen levels.[34] If D-dimers are high but fibrinogen remains normal, low molecular weight heparin (LMWH) may be indicated, particularly during high-risk periods like pregnancy or surgery. In cases where fibrinogen is low, hematological

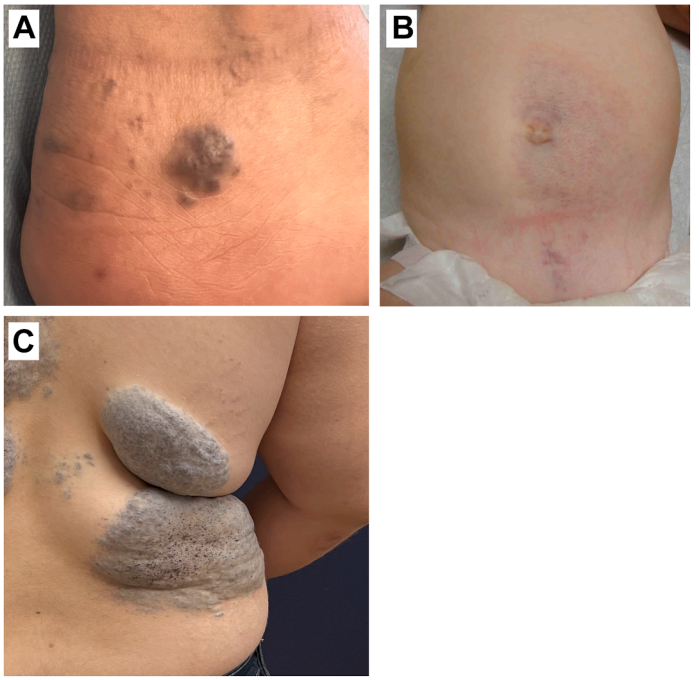

Fig. 8. (*A–C*) Clinical presentation of GVM (*A*) small cobblestone bluish lesion on the lateral side of the right ankle. (*B*) plaque-like type mimicking a capillary venous malformation on the abdomen. (*C*) Large GMV of the right lower back.

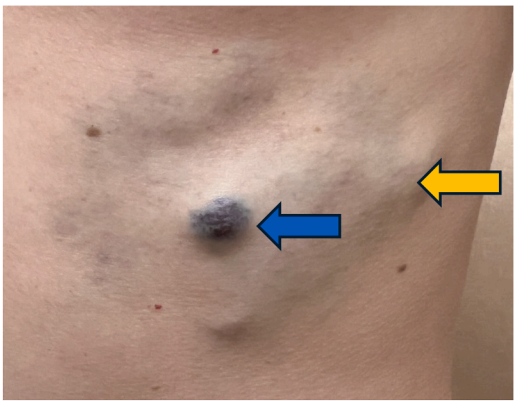

Fig. 9. Patient presenting with a VM of the left lower thoracic region. Notice the central cutaneous involvement (*blue arrow*) and surrounding only subcutaneous VM (*orange arrow*).

consughjltation is advised.[4] Furthermore, D-dimer level measurement serves as a cost-effective biomarker to distinguish multifocal VMs from other anomalies like lymphatic malformations, which typically present with normal levels.[34] D-dimer and fibrinogen tests are useful and highly specific to detect a venous component of a vascular anomaly (pure, combined, or syndromic).[4,34] GVM and other slow-flow vascular anomalies are not associated with LIC.[4,34]

Direct oral anticoagulants are currently being explored as a possible curative or preventive treatment for intravascular coagulopathy associated with VMs.[35,36] As oral contraceptives may increase thrombosis and chronic consumptive coagulopathy, a progesterone-only pill may be favored in patients with VMs.[4]

TREATMENT OF VENOUS MALFORMATIONS

VM is usually a chronic disease, and treatment should be tailored to each patient in a multidisciplinary experienced environment. Symptoms are key before discussing treatment options. As it is a benign lesion, treatment is not compulsory and should aim to treat symptoms rather than a radiological malformation. Even with no or minimal radiological difference, symptoms can be alleviated. Therapeutic options will vary according to specific subtypes and involved tissues (see **Fig. 5**, blue and dark brown boxes: Diffuse VM, Phlebectatic VM, According to involved tissue and specific subtypes), each treatment modality having its own benefits and risks (**Table 2**).

To measure treatment efficacy, pain evaluation and measurement is important as well as the evaluation of the QoL. Distinct questionnaires have been developed specifically for patients with vascular anomalies and should be used during consultation and follow-up.[32,33]

Conservative Management and Chronic Coagulopathy Treatment

Conservative management of VMs focuses on alleviating symptoms and preventing disease progression through noninvasive strategies, primarily centered on graded compression therapy to reduce blood stasis, limb volume, and the incidence of painful LIC. Anticoagulation can be proposed to treat painful LIC. LMWH is frequently the first-line treatment option but difficult to use in a chronic setting. Oral anticoagulants can be used for long-standing painful LIC.[37] Sirolimus is also associated with reduced D-dimer levels and can be proposed to treat LIC.[36,38,39]

Laser

Because of the larger vessel size and higher concentration of deoxyhemoglobin in VMs, the alexandrite and long-pulse Nd:YAG lasers are most commonly used.[40–42] Mucosal VMs are the most prone to be treated with laser. Care should be taken as to leave sufficient healthy mucosa between the laser pulses to avoid ulceration.[41] Superficial skin lesion can also be treated with Nd:YAG and interstitial Nd:YAG can be proposed to treat the malformation inside the tissues.[43–45]

Endovascular laser photocoagulation

Phlebectatic VMs may present with large, dilated veins and are at risk of causing pulmonary embolism in case of associated LIC. Those large draining veins can be targeted using endovascular laser photocoagulation which uses thermal effect to destroy endothelium and causes the vein to collapse.[46]

Interventional Radiology

Sclerotherapy

Interventional radiologic management of VMs relies predominantly on percutaneous sclerotherapy, which is widely accepted as a safe and effective first-line treatment aimed at symptom control, lesion reduction, or preoperative optimization. This technique is typically performed via ultrasound-guided direct needle puncture of the malformation, allowing intralesional contrast injection and digitally subtracted venography to delineate lesion architecture and venous drainage prior to sclerosant delivery.[47] A variety of sclerosant agents are available, each with distinct mechanisms of action, efficacy profiles, and risk–benefit

Table 2
Summary of benefits and risks for each available treatment option

Treatment Options	Advantages	Disadvantages and Risks
Conservative Management (compressive garments if on extremities)	Reduces blood stasis, limb volume, and incidence of painful localized intravascular coagulopathy (LIC)	Often not enough to relieve patient's symptoms
Anticoagulation		
LMWH	Useful to treat occasional thrombotic events; frequently used in a perioperative setting	Difficult to use in a chronic setting
DOAC	Efficient to treat chronic LIC	Adverse events linked to chronic anticoagulation; needs to be stopped before invasive treatment
Laser		
Laser therapy (Nd:YAG/ Alexandrite)	Particularly effective for mucosal VMs; interstitial Nd:YAG can treat deep tissue malformations	Risk of ulceration if healthy mucosa is not preserved between pulses
Endovascular laser	Uses thermal effects to destroy endothelium and collapse large phlebectatic veins	Only available for phlebectatic veins
Sclerotherapy	Safe and effective first-line treatment for symptom control and lesion reduction if performed by experienced interventional radiologist	Risks vary by agent; may include pain, skin necrosis, or hyperpigmentation
Absolute Ethanol	The most potent sclerosant available for rapid endothelial destruction	High morbidity, requires general anesthesia and has a ~10% complication rate
Bleomycin	High response rates with a favorable inflammatory profile; ideal for head and neck VMs	Risk of hyperpigmentation Be aware of cumulative toxicity
Electrosclerotherapy (BEST)	Seem to require fewer sessions then standard sclerotherapy	~10% complication rate, skin necrosis and prolonged swelling Risk of hyperpigmentation
Embolotherapy (Glue)	Simplifies surgical resection of deep, well-defined intramuscular lesions	Seldom used as a standalone treatment; creates an embolic cast
Cryotherapy	Minimally invasive; particularly used for FAVAs which respond less to sclerotherapy	No specific disadvantages noted in the source text other than use-case specificity
Surgical Resection	Can be curative for well-localized lesions; the primary option for glomuvenous malformations (GVM). Partial or staged resections are feasible	Visible postoperative scar or deformation. Electrocautery is often ineffective on pathologic walls
Targeted medical treatment	Can be used to treat extensive lesions; can treat LIC	Side effects linked to each specific medication
Sirolimus	High clinical improvement rate; provides rapid pain reduction, QoL benefits and disease stabilization	Frequent mild-to-moderate adverse events; requires long-term administration (1–2 y)
Alpelisib	Promising for PIK3CA-driven lesions; provides volumetric reduction and QoL benefits	Risk of hyperglycemia, diarrhea, and potential growth effects in children; long-term outcomes unknown

Abbreviations: BEST, bleomycin electrosclerotherapy; DOAC, direct anticoagulant; FAVA, fibro-adipose vascular anomaly; LIC, localized intravascular coagulopathy; LMWH, low molecular weight heparin; VM, venous malformation.

considerations. Sodium tetradecyl sulfate, an anionic detergent that disrupts endothelial cell membranes, is commonly administered as a foam, most often prepared using the Tessari technique with air and ethiodized oil (commonly known as lipiodol) to enhance fluoroscopic visibility, with reported symptomatic improvement in approximately two-thirds of treated patients, albeit with risks of pain, skin necrosis, and hyperpigmentation.[47] Absolute ethanol, which induces rapid endothelial destruction and protein denaturation leading to thrombosis, remains the most potent sclerosant but is associated with significant morbidity and requires general anesthesia.[48] It has a higher complication rate of around 10%.[45] To reduce this complication rate, a gelified form of ethanol has been developed.[49,50] Bleomycin, an antineoplastic antibiotic causing DNA strand breaks and endothelial disruption, offers high response rates with a more favorable inflammatory profile, making it particularly suitable for head and neck VMs where airway or orbital edema is a concern.[47,51] Long-term cumulative toxicity must be considered. Its efficacy may be further enhanced by electrosclerotherapy (see below). Polidocanol, another detergent-based sclerosant, represents a milder alternative characterized by slower endothelial injury and thrombosis, which reduces acute toxicity but increases the likelihood of recanalization; its use in foam form significantly improves endothelial contact, allows dose reduction, and achieves higher rates of lesion regression compared with liquid administration, positioning it as a useful option in anatomically sensitive regions or in staged treatment strategies.[52] Additional agents such as ethanolamine oleate and doxycycline are used selectively.[47]

Electrosclerotherapy

Bleomycin electrosclerotherapy (BEST) is a minimally invasive technique derived from electrochemotherapy that combines intralesional bleomycin with electroporation to treat slow-flow vascular malformations, enhancing intracellular drug delivery through transient increases in cell membrane permeability and thereby improving efficacy compared with conventional bleomycin sclerotherapy.[53] Clinical results reported to date are highly encouraging: mean lesion volume reductions of approximately 25% after a single session and up to 33% after completion of treatment have been documented, with symptomatic improvement observed in more than 90% of patients and complete symptom resolution in a smaller subset. BEST often achieves these results with 1 or 2 sessions rather than multiple procedures. The safety profile is generally favorable, with an overall complication rate of approximately 10% predominantly local side effects, including skin necrosis, prolonged swelling.[54,55] Systemic complications and allergic reactions are notably rare. Importantly, the markedly reduced bleomycin doses used in BEST compared with conventional sclerotherapy substantially limit the risk of cumulative toxicity, particularly pulmonary complications, supporting BEST as a promising but still evolving modality requiring further standardization and long-term evaluation.

Embolotherapy

Intravenous embolization with glue (n-butyl-2-cyanoacrylate) can be proposed but is seldom used alone. As opposed to sclerotherapy, embolotherapy will not empty the malformation and induce sclerosis but rather fill the intravascular space causing secondarily an endovascular sclerosing effect. It is used in combination with surgical resection, especially for deep intramuscular well-defined lesions that are much easier to find and resect after embolization.[56–61]

Cryotherapy

Percutaneous cryoablation is a minimally invasive treatment procedure that uses controlled freezing to treat VMs with probes that are placed under ultrasound guiding.[62] It is mostly used in FAVA, as they seem to respond less to sclerotherapy.[13,63,64]

Medical Treatment

Sirolimus and alpelisib represent 2 targeted systemic therapies acting at different levels of the PI3K–AKT–mTOR pathway for the treatment of slow-flow vascular malformations, with distinct indications, efficacy profiles, and safety considerations.[36] Sirolimus, an allosteric mTOR inhibitor, is currently the most established medical therapy for VMs, supported by prospective and large multicenter data, notably the VASE trial, which demonstrated clinical improvement in approximately 85% of patients, rapid pain reduction in nearly three-quarters within the first month, and meaningful functional and bleeding control across both TIE2- and PIK3CA-mutated malformations.[38,65] Treatment is typically administered for 1 to 2 years and can be discontinued in a substantial proportion of patients without relapse, suggesting disease stabilization rather than lifelong suppression. Although adverse events are frequent, they are predominantly mild to moderate, reversible with dose adjustment, and rarely lead to definitive discontinuation; importantly, fertility effects may be transient but are reversible after cessation.[36] Alpelisib, a selective PI3Kα inhibitor acting upstream, has emerged as a promising alternative particularly for

PROS and *PIK3CA*-driven vascular malformations,[66] supported by early clinical studies showing significant volumetric reduction, improved organ dysfunction, and QoL benefits, with radiological responses more pronounced in *PIK3CA*- than *TEK*-related lesions.[67] However, reported response rates remain heterogeneous, long-term outcomes are unknown, and toxicity differs from sirolimus, with higher rates of hyperglycemia, diarrhea, alopecia, and potential growth effects in children. In the absence of direct comparative trials and long-term safety data, sirolimus remains the first-line targeted therapy for most slow-flow vascular malformations, while alpelisib is best considered a second-line or mutation-specific option, particularly in refractory *PIK3CA*-driven disease.[36] More recently, a mutant-specific PI3K-alpha subunit inhibitor has emerged from the cancer field (zovegalisib, RLY-2608) which could reduce the side effects observed with alpelisib.[68] Its efficacy on *PIK3CA*-driven vascular anomalies is currently being tested in a phase-II clinical trial (NCT06789913).

Surgery

Surgical resection can either be complete or partial. A complete surgical resection of a VM will be proposed for well localized lesions, easily accessible and with limited postoperative sequalae.[69] In case of diffuse intramuscular VM, limited to one muscle or one fascial compartment, complete resection of the involved muscle of its compartment can be proposed. Surgical resection is frequently proposed to treat GVMs, as they seem to respond less to either sclerotherapy, with a higher risk of skin necrosis,[70] or medical treatments then VMs. FAVA can be resected partially or completely. HCCVM or VVM, when symptomatic, can be surgically removed. Complete surgical resection is rarely feasible and partial or sequential resections can be proposed. In large lesions, the affected areas will need to be reconstructed with split thickness skin grafts. In those cases, postoperative recurrence of the initial bluish discoloration is frequently observed on the edges of the skin grafts, but without the hyperkeratotic component alleviating preoperative symptoms. Intraarticular VMs, frequently seen in Bockenheimer disease, need to be treated before cartilaginous lesions appear due to small recurrent bleedings from the malformation.[71–73] If symptomatic, phleboliths can be excised as well as fibrosis secondary to sclerotherapy.

If complete surgical resection is not feasible, partial resections can be proposed. When a partial resection is planned, LIC must be excluded preoperatively, assessed by measurement of D-dimer and fibrinogen levels. In cases of LIC, LMWH (100 anti-Xa IU/kg/day) should be initiated preoperatively when fibrinogen levels are reduced or if D-dimer levels are above 5 times the normal range, and continued for 2 weeks postoperatively; in this context, hematology consultation is advisable to optimize management. Intraoperative hemostasis should preferentially rely on ligation rather than electrocautery, which is frequently ineffective on pathologic venous walls. Intravenous tranexamic acid is effective in cases of abnormal intraoperative bleeding. Topical application of thrombin-based hemostatic agents to the surgical site is recommended to reduce postoperative oozing and hematoma formation.[69] To manage the remaining VM in partial resection, a squeezing technique can be used. It consists of segmental compression ("sausage-like" partitioning) of the VM using transfixing running sutures with nonabsorbable material (polypropylene). The remaining abnormal vessels will not be able to fill in with blood and will progressively form fibrosis. However, it is ineffective in limb involvement, where pain often persists.

Staged and Multidisciplinary Management

Sclerotherapy is usually the first-line treatment, but in many cases multidisciplinary management is needed, either with combined therapeutic modalities or sequential treatment options (**Fig. 10**). Preoperative sclerotherapy will reduce the amount of blood inside the malformation and cause sclerosis which can be easier to resect then friable abnormal veins as found in previously untreated VMs. Preoperative embolotherapy will allow to reduce peroperative bleeding and easier palpation of intramuscular VMs. The vase trial showed that medical treatment can, in some cases, reduce the volume of a diffuse VM and allow partial surgical resection or sclerotherapy that was not possible beforehand.[38] In case of partial resections in large or diffuse VMs, perioperative concomitant sirolimus treatment should be considered.

CONCLUSION

VMs encompass a diverse range of subtypes, which can either be combined with other slow-flow malformations or be part of a specific syndrome. These malformations can occur anywhere on the body, and treatment approaches vary depending on the specific subtype and the tissues involved. Effective management of VMs requires a multidisciplinary, experienced environment that provides a comprehensive range of therapeutic modalities to address these, sometimes complex, vascular anomalies. This allows for frequent and

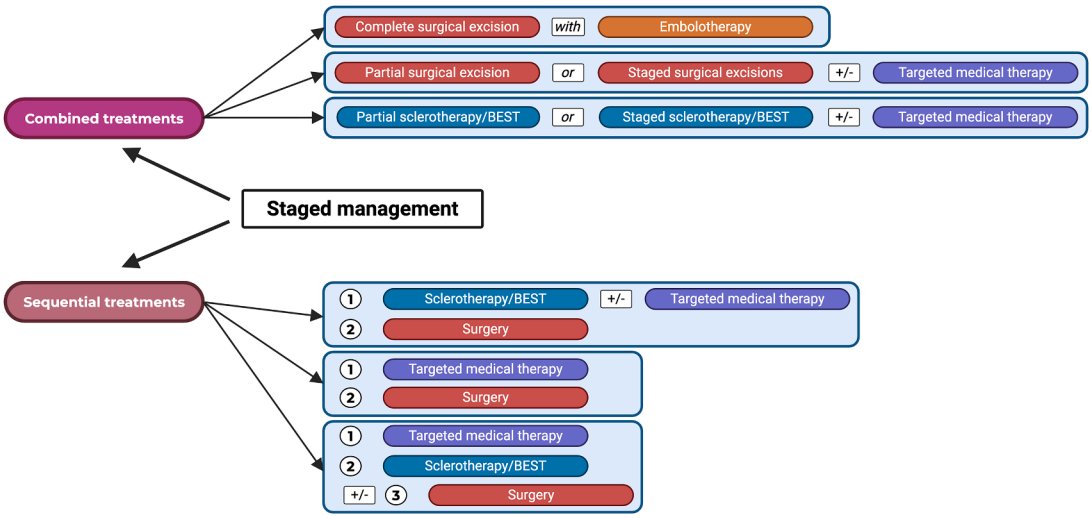

Fig. 10. Schematic representation of the different combinations of multimodal treatment modalities in staged management of VMs.

effective combinations of different treatment options.

SUMMARY

VMs represent a prevalent category of slow-flow vascular anomalies, estimated to affect 1 in 2000 to 5000 individuals, and originate from the aberrant development of venous channels with disorganized smooth muscle cell layering. These lesions are primarily driven by the hyperactivation of the TIE2-PI3K-AKT-mTOR signaling pathway. The clinical spectrum is broad, encompassing isolated VMs, which may be spongiform or phlebectatic, and specialized variants such as VVM, FAVAs, and the extensive Bockenheimer disease. Multifocal presentations can be sporadic, as seen in MSVMs, BRBNS, or hereditary, such as VMCM, HCCVM, VMOS, and GVMs, the latter of which are uniquely characterized by painful, noncompressible nodules containing glomus cells. Diagnosis can be guided by genetic testing and otherwise relies on clinical evaluation and imaging, with MRI serving as the gold standard to delineate anatomic involvement, while ultrasound confirms the slow-flow nature of the lesion. A critical component of management is the monitoring of LIC, identified by elevated D-dimer levels, which can progress to DIC during surgical interventions. Therapeutic strategies are multidisciplinary and symptom-driven, utilizing conservative measures like graded compression, interventional radiology such as sclerotherapy, surgical resections, and targeted medical therapies. Different therapeutic modalities can be combined or sequentially used in a staged management strategy.

CLINICS CARE POINTS

- Doppler US is the gold standard complementary examinations for the diagnosis of VMs.
- MRI is required for the more precise location and extension of VMs if treatment considered.
- LIC should be excluded before considering invasive treatments. In case of lowered fibrinogen or D-dimer more than 5 times above the normal range, anticoagulation needs to be initiated beforehand.
- Genetic testing can help defining the specific VM subtype.
- All small well-localized VM subtypes can be surgically removed.
- Superficial and mucosal VMs can be treated with laser therapy.
- Phlebectatic VMs can be treated with endovascular laser therapy.
- GVMs seem to respond less to sclerotherapy or medical treatments. If symptomatic, they can be surgically removed or treated with laser therapy.
- FAVAs do not respond well to sclerotherapy or medical treatments. If symptomatic, surgical excision or cryotherapy can be proposed.
- Surgical resection of intramuscular VMs can be made easier with preoperative glue embolization.
- Hyperkeratotic skin lesions as seen in VVM and HCCVM can be surgically removed, but local discoloration recurrence can occur.
- Diffuse VMs can be partially resected and staged surgical resection can be planned. In

case of partial treatments, perioperative sirolimus administration should be considered.

- Preoperative sclerotherapy can reduce the amount of venous blood inside the lesion and allow to resect resulting fibrotic tissues.

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REFERENCES

1. Seront E, Vikkula M, Boon LM. Venous malformations of the head and neck. Otolaryngol Clin North Am 2018;51(1):173–84.
2. Goldenberg DC, Vikkula M, Penington A, et al. Updated classification of vascular anomalies: a living document from the International Society for the Study of Vascular Anomalies Classification Group. J Vasc Anom 2025;6(2):e113.
3. Dompmartin A, Vikkula M, Boon LM. Venous malformation: update on aetiopathogenesis, diagnosis and management. Phlebology 2010;25(5):224–35.
4. Dompmartin A, Baselga E, Boon LM, et al. The VASCERN-VASCA working group diagnostic and management pathways for venous malformations. J Vasc Anom 2023;4(2):e064.
5. Mulliken JB, Burrows PE, Fishman SJ, et al. Mulliken and young's vascular anomalies: Hemangiomas and malformations. 2nd edition. Oxford: Oxford University Press; 2013.
6. Soblet J, Limaye N, Uebelhoer M, et al. Variable somatic TIE2 mutations in half of sporadic venous malformations. Mol Syndr 2013;4(4):179–83.
7. Limaye N, Kangas J, Mendola A, et al. Somatic activating PIK3CA mutations cause venous malformation. Am J Hum Genet 2015;97(6):914–21.
8. Couto JA, Vivero MP, Kozakewich HPW, et al. A somatic MAP3K3 mutation is associated with verrucous venous malformation. Am J Hum Genet 2015;96(3):480–6.
9. Tennant LB, Mulliken JB, Perez-Atayde AR, et al. Verrucous hemangioma revisited. Pediatr Dermatol 2006;23(3):208–15.
10. Wang L, Gao T, Wang G. Verrucous hemangioma: a clinicopathological and immunohistochemical analysis of 74 cases. J Cutan Pathol 2014;41(11):823–30.
11. Schmidt BAR, El Zein S, Cuoto J, et al. Verrucous venous malformation—subcutaneous variant. Am J Dermatopathol 2021;43(12). Available at: https://journals.lww.com/amjdermatopathology/fulltext/2021/12000/verrucous_venous_malformation_subcutaneous_variant.49.aspx.
12. Alomari AI, Spencer SA, Arnold RW, et al. Fibro-adipose vascular anomaly: clinical-radiologic-pathologic features of a newly delineated disorder of the extremity. J Pediatr Orthop 2014;34(1):109–17.
13. Shaikh R. Fibroadipose vascular anomaly: diagnosis and treatment. Tech Vasc Interv Radiol 2024;27(2):100961.
14. Hori Y, Hirose K, Ozeki M, et al. PIK3CA mutation correlates with mTOR pathway expression but not clinical and pathological features in Fibro-adipose vascular anomaly (FAVA). Diagn Pathol 2022;17(1):19.
15. Ali B, Panossian A, Taghinia A, et al. Diffuse venous malformations of the upper extremity (bockenheimer disease): diagnosis and management. Plast Reconstr Surg 2020;146(6):1317–24.
16. Sudduth CL, Konczyk DJ, Smits PJ, et al. Bockenheimer disease is associated with a *TEK* variant. Mol Case Stud 2021;7(6):a006119.
17. Revencu N, Coulie J, Boon LM, et al. Genetic aspects of vascular malformations. Presse Med 2025;54(3):104295.
18. Soblet J, Kangas J, Natynki M, et al. Blue rubber bleb nevus (BRBN) syndrome is caused by somatic TEK (TIE2) mutations. J Invest Dermatol 2017;137(1):207–16.
19. Seront E, Boon LM, Vikkula M. TEK-related venous malformations. In: Adam MP, Bick S, Mirzaa GM, et al, editors. GeneReviews®. Seattle (WA): University of Washington, Seattle; 2008. p. 1993–2025.
20. Wouters V, Limaye N, Uebelhoer M, et al. Hereditary cutaneomucosal venous malformations are caused by TIE2 mutations with widely variable hyper-phosphorylating effects. Eur J Hum Genet 2010;18(4):414–20.
21. Boon LM, Ballieux F, Vikkula M. Vascular malformations. In: Kang S, Amagai M, Bruckner AL, et al, editors. Fitzpatrick's dermatology, 9e. McGraw-Hill Education; 2019. Available at: accessmedicine.

mhmedical.com/content.aspx?aid=1161350730. Accessed January 2, 2026.
22. Sirvente J, Enjolras O, Wassef M, et al. Frequency and phenotypes of cutaneous vascular malformations in a consecutive series of 417 patients with familial cerebral cavernous malformations. J Eur Acad Dermatol Venereol 2009;23(9):1066–72.
23. Baranoski JF, Lawton MT. Cerebral cavernous malformations. In: Mascitelli JR, Binning MJ, editors. Introduction to vascular neurosurgery. Cham, Switzerland: Springer International Publishing; 2022. p. 457–70. https://doi.org/10.1007/978-3-030-88196-2_24.
24. Boon LM, Mulliken JB, Enjolras O, et al. Glomuvenous malformation (glomangioma) and venous malformation: distinct clinicopathologic and genetic entities. Arch Dermatol 2004;140(8):971–6.
25. Brouillard P, Boon LM, Revençu N, et al. Genotypes and phenotypes of 162 families with a glomulin mutation. Mol Syndromol 2013;4(4):157–64.
26. Cetinkaya A, Xiong JR, Vargel İ, et al. Loss-of-Function mutations in ELMO2 cause intraosseous vascular malformation by impeding RAC1 signaling. Am J Hum Genet 2016;99(2):299–317.
27. Mitova N, Petkova-Ninova V, Bakardjiev P. Primary intraosseous vascular malformation in a child with ELMO2 mutation: diagnostic and dental management challenges. Dent J 2025;13(10):473.
28. Pansuriya TC, Van Eijk R, d'Adamo P, et al. Somatic mosaic IDH1 and IDH2 mutations are associated with enchondroma and spindle cell hemangioma in Ollier disease and maffucci syndrome. Nat Genet 2011;43(12):1256–61.
29. Keppler-Noreuil KM, Rios JJ, Parker VER, et al. *PIK3CA* -related overgrowth spectrum (PROS): diagnostic and testing eligibility criteria, differential diagnosis, and evaluation. Am J Med Genet A 2015;167(2):287–95.
30. Olivieri B, White CL, Restrepo R, et al. Low-flow vascular malformation pitfalls: from clinical examination to practical imaging evaluation—part 2, venous malformation mimickers. Am J Roentgenol 2016;206(5):952–62.
31. Vogel SA, Hess CP, Dowd CF, et al. Early versus later presentations of venous malformations: where and why? Pediatr Dermatol 2013;30(5):534–40.
32. Horbach SER, Van Der Horst CMAM, Blei F, et al. Development of an international core outcome set for peripheral vascular malformations: the OVAMA project. Br J Dermatol 2018;178(2):473–81.
33. England RW, Motaghi M, Kohler B, et al. Development and preliminary validation of the patient-reported outcome measure for vascular malformation questionnaire: a prospective cohort study. J Vasc Interv Radiol 2021;32(5):683–90.e4.
34. Dompmartin A, Acher A, Thibon P, et al. Association of localized intravascular coagulopathy with venous malformations. Arch Dermatol 2008;144(7):873–7.
35. Ardillon L, Lambert C, Eeckhoudt S, et al. Dabigatran etexilate versus low-molecular weight heparin to control consumptive coagulopathy secondary to diffuse venous vascular malformations. Blood Coagul Fibrinolysis 2016;27(2):216–9.
36. Seront E, Hermans C, Boon LM, et al. Targeted treatments for vascular malformations: current state of the art. J Thromb Haemost 2024;22(11):2961–75.
37. Lagneaux E, Boon LM, Revencu N, et al. Direct oral anticoagulants and venous malformations: literature review and retrospective study of 29 patients. Res Pract Thromb Haemost 2024;8(3):102400.
38. Seront E, Van Damme A, Legrand C, et al. Preliminary results of the European multicentric phase III trial regarding sirolimus in slow-flow vascular malformations. JCI Insight 2023;8(21):e173095.
39. Mack JM, Verkamp B, Richter GT, et al. Effect of sirolimus on coagulopathy of slow flow vascular malformations. Pediatr Blood Cancer 2019;66(10):e27896.
40. Murthy AS, Dawson A, Gupta D, et al. Utility and tolerability of the long-pulsed 1064-nm neodymium:yttrium-aluminum-garnet (LP Nd:YAG) laser for treatment of symptomatic or disfiguring vascular malformations in children and adolescents. J Am Acad Dermatol 2017;77(3):473–9.
41. DeHart AN, Richter GT. Laser treatment of vascular anomalies. Dermatol Clin 2022;40(4):481–7.
42. Spradley TP, Johnson AB, Wright HD, et al. Modified ND:YAG laser therapy in the treatment of cutaneous venous malformations. Facial Plast Surg Aesthetic Med 2021;23(4):289–93.
43. Sarig O, Kimel S, Orenstein A. Laser treatment of venous malformations. Ann Plast Surg 2006;57(1):20–4.
44. Poetke M, Philipp CM, Urban P, et al. Interstitial laser treatment of venous malformations. Med Laser Appl 2001;16(2):111–9.
45. Van Der Vleuten CJM, Kater A, Wijnen MHWA, et al. Effectiveness of sclerotherapy, surgery, and laser therapy in patients with venous malformations: a systematic review. Cardiovasc Interv Radiol 2013. https://doi.org/10.1007/s00270-013-0764-2.
46. Reis J, Alomari AI, Trenor CC, et al. Pulmonary thromboembolic events in patients with congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and spinal/skeletal abnormalities and Klippel-Trénaunay syndrome. J Vasc Surg Venous Lymphat Disord 2018;6(4):511–6.
47. Patel ND, Chong AT, Kolla AM, et al. Venous malformations. Semin Interv Radiol 2022;39(05):498–507.
48. Hammer FD, Boon LM, Mathurin P, et al. Ethanol sclerotherapy of venous malformations: evaluation of systemic ethanol contamination. J Vasc Interv Radiol 2001;12(5):595–600.
49. Dompmartin A, Blaizot X, Théron J, et al. Radio-opaque ethylcellulose-ethanol is a safe and efficient

sclerosing agent for venous malformations. Eur Radiol 2011;21(12):2647–56.
50. Wohlgemuth WA, Müller-Wille R, Teusch V, et al. Ethanolgel sclerotherapy of venous malformations improves health-related quality-of-life in adults and children – results of a prospective study. Eur Radiol 2017;27(6):2482–8.
51. Bertino F, Trofimova AV, Gilyard SN, et al. Vascular anomalies of the head and neck: diagnosis and treatment. Pediatr Radiol 2021;51(7):1162–84.
52. Ali S, Mitchell S. Outcomes of venous malformation sclerotherapy: a review of study methodology and long-term results. Semin Interv Radiol 2017;34(03): 288–93.
53. Muir T, Bertino G, Groselj A, et al. Bleomycin electrosclerotherapy (BEST) for the treatment of vascular malformations. An International Network for Sharing Practices on Electrochemotherapy (InspECT) study group report. Radiol Oncol 2023;57(2):141–9.
54. Deleu A, Brill R, Schüngel MS, et al. Prospective analysis of bleomycin electrosclerotherapy for clinical outcome and volume reduction in therapy refractory slow-flow malformations. CVIR Endovasc 2025;8(1):121.
55. Schmidt VF, Cangir Ö, Meyer L, et al. Outcome of bleomycin electrosclerotherapy of slow-flow malformations in adults and children. Eur Radiol 2024;34-(10):6425–34.
56. Tyagi I, Syal R, Goyal A. Management of low-flow vascular malformations of upper aero digestive system—role of N-butyl cyanoacrylate in peroperative devascularization. Br J Oral Maxillofac Surg 2006; 44(2):152–6.
57. Cil BE, Vargel I, Geyik S, et al. Venous vascular malformations of the craniofacial region: pre-operative embolisation with direct percutaneous puncture and *N* -butyl cyanoacrylate. Br J Radiol 2008;81-(972):935–9.
58. Tieu DD, Ghodke BV, Vo NJ, et al. Single-stage excision of localized head and neck venous malformations using preoperative glue embolization. Otolaryngol Neck Surg 2013;148(4):678–84.
59. Uller W, El-sobky S, Alomari AI, et al. Preoperative embolization of venous malformations using *n* -Butyl cyanoacrylate. Vasc Endovascular Surg 2018;52(4): 269–74.
60. Chewning RH, Monroe EJ, Lindberg A, et al. Combined glue embolization and excision for the treatment of venous malformations. CVIR Endovasc 2018;1(1):22.
61. Puccia R, Staricha K, Carlberg VM, et al. Utilizing immediate preoperative n-BCA in the resection of head and neck venous and lymphatic malformations. Int J Pediatr Otorhinolaryngol 2020;138:110388.
62. Ramaswamy RS, Tiwari T, Darcy MD, et al. Cryoablation of low-flow vascular malformations. Diagn Interv Radiol 2019;25(3):225–30.
63. Shaikh R, Alomari AI, Kerr CL, et al. Cryoablation in fibro-adipose vascular anomaly (FAVA): a minimally invasive treatment option. Pediatr Radiol 2016; 46(8):1179–86.
64. Marcelin C, Linet T, Jambon E, et al. Percutaneous image-guided cryoablation of venous malformation and fibro-adipose vascular anomaly: prognostic factors of clinical efficacy. Eur Radiol 2025. https://doi.org/10.1007/s00330-025-11545-w.
65. Eng W. Targeted medical therapies for vascular anomalies: a clinical review. Am J Med Genet C Semin Med Genet 2025;199(3):161–75.
66. Pithadia DJ, Heskel MJ, Shotayev A, et al. Alpelisib, a PI3Kα inhibitor, effectively treats vascular anomalies with diverse genotypes and phenotypes. Blood Vessels Thromb Hemost 2026;3(1):100133.
67. Venot Q, Blanc T, Rabia SH, et al. Targeted therapy in patients with PIK3CA-related overgrowth syndrome. Nature 2018;558(7711):540–6.
68. Tyrakis PA, Kampjut D, Steele GF, et al. Multi-node inhibition targeting mTORC1, mTORC2 and PI3Kα potently inhibits the PI3K/AKT/mTOR pathway in endometrial and breast cancer models. Br J Cancer 2025;133(2):144–54.
69. Coulie JBL. Indications chirurgicales des malformations vasculaires. EMC Tech Chir Chir Plast Reconstr Esthét 2019;14(2):1–15.
70. Mounayer C, Wassef M, Enjolras O, et al. Facial "glomangiomas": large facial venous malformations with glomus cells. J Am Acad Dermatol 2001;45(2): 239–45.
71. Pireau N, Boon LM, Poilvache P, et al. Surgical treatment of intra-articular knee venous malformations: when and how? J Pediatr Orthop 2016;36(3):316–22.
72. Laurian C, Masonni C, Wassef M, et al. Surgical treatment of venous malformations of the knee: treatment outcomes for 35 patients. J Pediatr Orthop 2018;38(6):e325–31.
73. Jones KM, Corey KC, Garza-Mayers AC, et al. Classification of lower extremity venous malformations and risk of knee involvement: a retrospective cohort study. J Am Acad Dermatol 2021;85(6):1480–5.