Investigations in Vascular Malformations

11

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Vascular malformation is a complex clinical condition with myriad manifestations resulting from a variety of vascular lesions due to proliferative endothelium resulting from embryonic dysmorphogenesis. Clinical evaluation (Fig. 11.1) without imaging modality is never sufficient to classify categorically for complete diagnosis and guiding the treatment plan. Vascular endothelial lining of veins, arteries, lymphatics, or combined structures in skin, subcutaneous tissue, muscles, bones, or deep inside abdominal viscera may give rise to vascular malformations in various forms which need imaging evaluation (DUS, CT, MRI) always for complete diagnosis and treatment. The commonest location in the body is the head and neck region (40%), followed by extremities (40%) and trunks (20%) [1]. Prevalence of vascular malformations is about 4.5% with peripheral vascular malformations in population 0.8–1% [2, 3].

Investigations are essential for definite diagnosis in detail and imaging is a central component with first and foremost being non-invasive evaluation with DUS, CT, and MRI. The first diagnostic tool after the clinical evaluation is duplex ultrasonography (DUS) examination which is widely used for initial screening, but essential in all cases for planning treatment and further imaging assessment with B-mode for morphologic study and spectral, color, and power Doppler to find out flow characteristics [4].

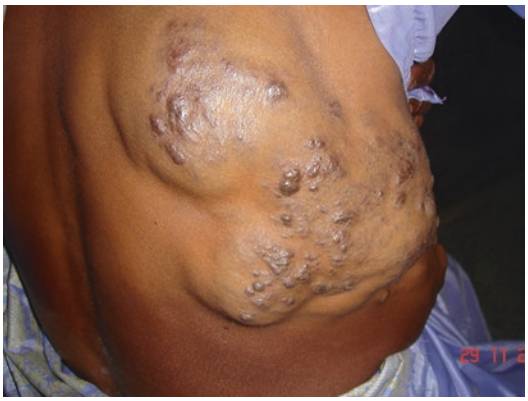

Fig. 11.1 Vascular malformation chest wall

The second line investigations are MRI and CT without or with contrast which allow a better morphologic study and lucid hemodynamic data and either of the above combined with DUS in most cases.

The third group in the line of examinations includes different tests performed mainly after the former two, decided by the data derived. It includes lymphoscintigraphy, whole blood pool scintigraphy, transarterial lung perfusion scintigraphy, bone scanogram.

The fourth and last panel is the invasive tests group, including catheter angiography which is used during the therapeutic session rather than

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diagnostic tool, phlebography, and lymphography which are used rarely nowadays.

11.1 Non-Invasive Diagnostic Tools

11.1.1 Duplex Ultrasound (DUS)

In the diagnostic dilemma of vascular malformations, duplex ultrasound remains basic, screening, most widely used and primary investigation practiced in all cases. The role of DUS is more and more due to the large scale availability of the equipment, low cost, lack of radiation exposure, lack of invasiveness, and the real-time investigation. Assessment of morphology and hemodynamic features are two outcomes after duplex study helping to plan further investigations or final therapeutics. Size of the vascular malformation can be derived always. The limiting point in the investigation is the limited special resolution. Very high temporal resolution facilitates real-time examinations and an accurate hemodynamic assessment. Limiting factors in DUS is the dependency on the operator, and finding in the investigation are related to knowledge of anatomy and pathology in addition to technical skills. There is some agreement for the necessity to standardize the examination and to perform it according to different depths [5].

Ultrasound is a good screening tool but it has limitations in defining the extent of lesions not located in the extremities and it is essential to supplement ultrasound assessment with MRI evaluation. Deep intramuscular lesions are best detected by MRI which may help in locating the lesion on ultrasound. The biggest challenge in Ultrasound investigations is examination in presence of air (e.g., lungs) or when lesions are located within bones. CT has an upper edge in the evaluation of Bony anomalies which may be the imaging modality of choice for lesions inside the bones. Limitations in the hemodynamic evaluation of venous status with USG can be compensated with intravascular pressure measurement and/or intravascular ultrasound (IVUS). However, it is always a rule to do IVUS or invasive pressure measurements only in selective cases and preferred with definitive intervention only but not as a routine procedure.

11.2 Duplex Ultrasound (DUS) Examination Procedure

Basic Principles

Clinical presentations should be in the background briefly with the time of onset, family history, and rate of progression before evaluating and interpreting ultrasound findings. Contralateral side should be examined to search occult malformations and to compare the morphology and hemodynamics. In unilateral lesions, complete clinical examination of contralateral side and Duplex USG comparison of both sides to identify normal size and structures is the key principle. Limbs should be examined both in erect and supine positions in all case with the recording of and the difference in size of the vessels.

Continuous Wave(CW)-Doppler Localization:

First assessment with CW-Doppler is recommended:

(a) To localize the lesion
(b) To determine the basic flow characteristics and
(c) To guide the duplex examination

Probe Selection

Most superficial lesions are assessed with linear probe of high frequency and pressure applied by probe should be minimum over the thick layer of ultrasound gel to avoid distortion and compression of the lesion. The advantage with using broadband transducers should be optimized to obtain the best image. When assessing facial lesions or anomalies in neonates and small children, a “hockeystick” probe may be selected. In case of superficial lesions, minimum pressure should be applied to the probe using a thick layer of ultrasound gel to prevent excessive compression on the lesion.

Salient Evaluation

The ultrasound examination should aim to achieve the following four key procedural outcomes [6, 7]:

1. Lesion: Diagnosis, Dimension, and Definite Classification
2. Localization and relationship with regional structures
3. Location: Compete mapping pre-operatively
4. Long term outcome: Post-intervention follow-up studies

11.2.1 Define the Lesion: Diagnosis, Dimension, and Definite Classification

Aims

(a) To recognize the presence of a vascular anomaly
(b) To differentiate between vascular tumor and malformation
(c) To classify as a high flow (AVM), low flow (VM), or no flow (LM) lesions
(d) To document the dimensions of the lesion and flow characteristics

B-Mode

First-hand tool in Duplex Study is the B-mode examination and it should be done before the Doppler examination. Initial assessment with B-Mode identifies either collection of vessels or cystic spaces or soft tissue mass or adjacent structures like nerve trunks. Compressibility on B-mode differentiate

(a) VM (compressible).
(b) Thrombosed or sclerosed VM (non-compressible).
(c) LM (non-compressible cystic spaces) and.
(d) AVMs (partially compressible).

B-mode will help in the evaluation of axial trunks and its patency, duplication, aplasia, hypoplasia, hyperplasia, valves in whole length, or in the localized segment. Outside the vessel, information about surrounding structures regarding echogenicity, regularity, the plane of separation may be obtained [8].

11.2.1.1 Doppler Mode (Color Doppler and Spectral Analysis)

Doppler assessment determines either flow within the lesion (active tumors, AVMs, VMs) or no flow at all (LMs, involuted tumors, thrombosed/sclerosed VMs). Flow within the lesion may be either induced (VMs) or spontaneous (AVMs). The examination includes both Color Doppler and Spectral analysis. For examination in the color mode examination, the pulse repetition frequency (PRF) is set to the flow velocity of the target vessel, i.e., PRF is increased for arterial flow and decreased for venous flow in VMs. Assessing high flow malformations, the setting of the color Doppler should be set on real time always without delay. Low amplitude flows better detected in Power Doppler as it is more sensitive than Color Doppler.

Spontaneous and augmented blood flow are detected in spectral analysis with Peak velocity and the Resistive Index (RI) in arterial vessels ([peak systolic velocity–end diastolic velocity] / peak systolic velocity) documentation always.

Reflux time is the key finding in venous Doppler examination and should be included always in venous examination mapping of the veins in the lower limb.

11.2.1.2 Diagnosis and Definite Classification

B-Mode and Doppler Mode study should be combined for a definite diagnosis and complete classification.

11.2.1.3 Dimension

The lesion should be measured and documented in all dimensions with an adequate number of B-mode images and definite morphology must be derived after demonstrating the basic features in the lesion should be obtained. Size, number, flow, and the hemodynamic characteristics of the lesion are recorded to monitor the course of the disease in terms of progression, the natural evolution, outcome either with success or failure of the treatment [9].

11.2.2 Localization and Relationship with Regional Structures

Localization of the lesion with documentation of the relationship with the regional blood vessels, nerves, muscles, and fascia (Fig. 11.2). Derived data should be a guiding factor for further investigations like MRI or CT. Both clinical and ultrasound examination should be combined for localization of the lesion with documentation of important landmarks in adjoining tissue structures.

Structures in the vicinity to the lesion should be identified ideally, assessed adequately with all vessels including arterial, venous, lymphatic along with adjoining structures including nerves, fascia, tendons, and muscles should be included in documentation. Nearby normal vascular structures along with normal opposite side examination is essential for evaluation of the size and flow of the vascular malformation. Architectural triad (Fig. 11.3) in VMs Afferent arterial "feeders," Efferent "draining" veins, and connecting central nidus should be delineated [10–12]). Ultrasound findings should guide further investigations like MRI in selected lesions only for complete diagnosis and subsequent therapeutic plan, protocol, and procedure.

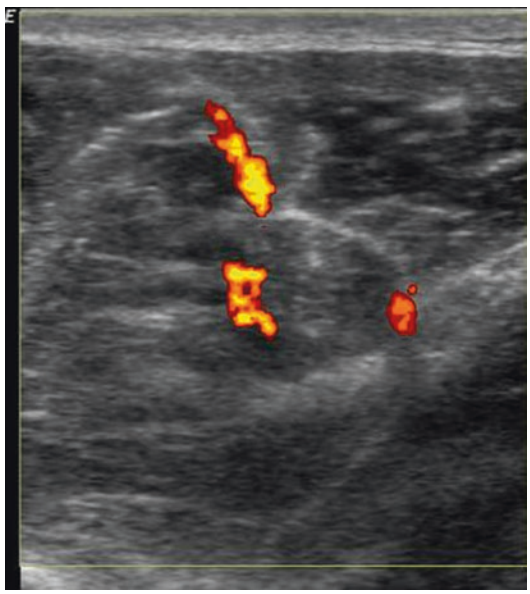


Fig. 11.2 Tiny serpentine anechoic channels (venous malformations) are noted in duplex scan involving posterior fibers of the deltoid muscle. Few echogenic foci are noted within phleboliths. Low-flow signals are noted

11.2.3 Location: Complete Pre-Operative Mapping

Therapeutic approach to target the lesion is always guided by complete pre-operative mapping with identification and marking of all important adjoining structures like arteries, veins, nerves, tendons, ligaments, muscles with proper identification of feeding arteries and draining veins and any other communications with the vascular system.

Complete and comprehensive duplex assessment should be complemented by surface markings over the skin to guide the site of vascular approach and plan of treatment. Significant surrounding structures should be documented and marked on the skin. Neural protection should be in each and every case with the identification of nerve trunks before intervention as damage to the nerve may be devastating which is a dreaded complication of endovascular or surgical procedures performed for vascular malformations. Direct puncture, the direct effect of therapeutic agents like sclerosant or embolic agent, or diffuse edema after intervention leading to compartment syndrome may cause nerve damage.

11.2.4 Long Term Outcome (Follow-Up Studies): Complications/Success/Failure

Follow-up study to analyze outcome in terms of complications, success, or failure of therapy is screened always by ultrasound in almost all cases. Residual and recurrent disease is the most significant phenomenon associated with vascular malformations which are detected during follow-up with the use of ultrasound. Early complications like DVT develops within days and to detect it earliest USG is advised within the first week of intervention.

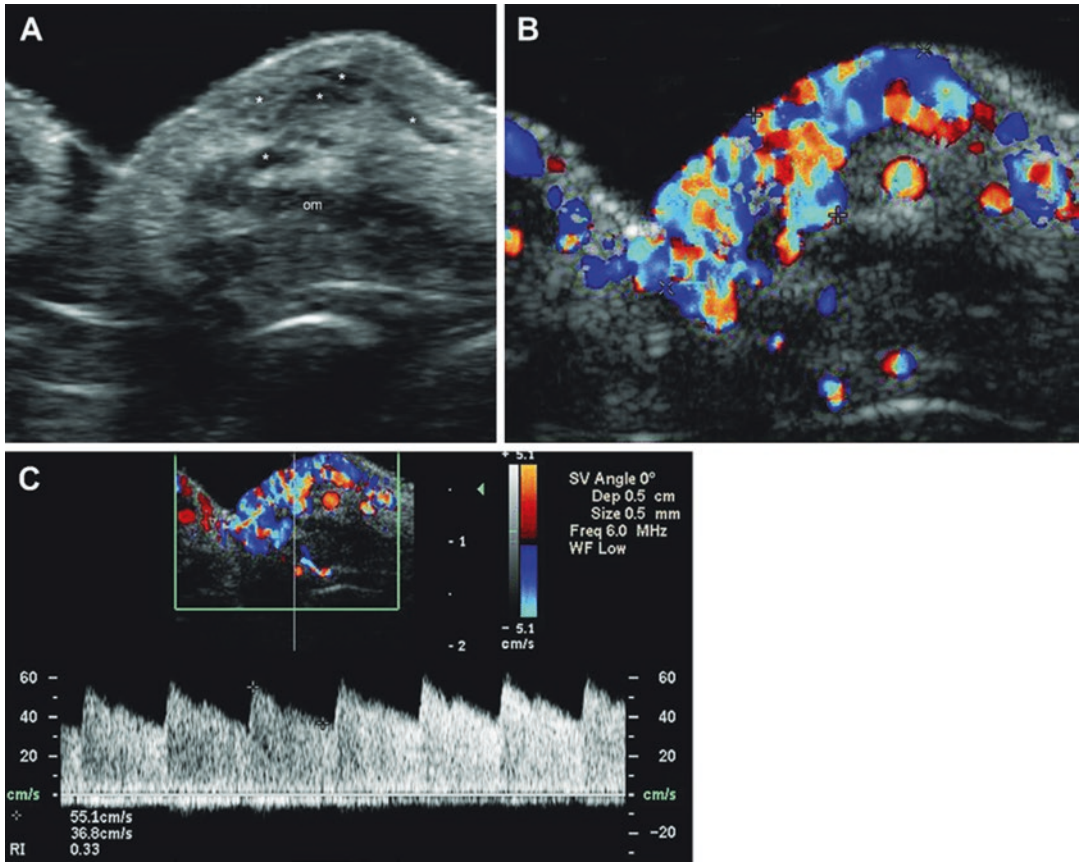


Fig. 11.3 High-flow-arterial-vascular-malformation-lower-lip-A-Gray-scale-longitudinal-view

Ultrasound examinations during long term follow-up should follow the same protocol as for the initial assessment,

This should include:

(a) B-mode images of lesion
(b) Measurements of the size and
(c) Flow
(d) Transverse dual image of the lesion to assess for compressibility
(e) Color Doppler images of the lesion and
(f) Sample spectral traces in associated vessels and nidus

11.2.4.1 Success/Failure of Endovascular Interventions

Compressibility is the key parameter in USG examination for evaluation of the vascular malformations but it loses its importance after endovascular intervention as it has a limitation in assessing the success of the therapy. Treated lesions are sclerosed or thrombosed and may not be compressible despite residual flow containing lesions which is assessed by Color Doppler study.

11.3 Venous Malformation (VM): Key Points

Venous Malformations (VMs) are anomalies of the venous system classified as truncular or extra-truncular [11, 12]. It is either isolated or may be associated with other malformations like Lymphatic(LM), Capillary(CM), Arteriovenous(AVM), or generalized syndromes(KTS).

11.4 Lymphatic Malformations (LM): Key Points

LMs are classified in truncular malformations and extratruncular lesions. LMs may be isolated or combined with others like CMs, VMs, and AVMs or as part of a generalized syndrome-like KTS.

Truncular LMs are may be due to agenesis, aplasia, hypoplasia, or hyperplasia/dilatation of the lymphatic vessels. Clinically presentation of truncular LMs manifests as primary lymphedema while Extratruncular lesions present as macrocytic or microcystic lesions. Division in macrocystic and microcystic is based on size which is less than 2 cm for microcystic and more than 2 cm for macrocystic. Fluid overload in soft tissues is always present in truncular lesion causing lymphedema [13, 14].

Central and key tool in the assessment of LMs remains Ultrasound which may be supplemented with lymphoscintigraphy(LSG). LSG is the gold standard in the study of the lymphodynamics in truncular lymphatic malformations. Ultrasonography in LMs is comparable with the information revealed by MRI.

Skin thickness measurement is the most important parameter in LMs to assess and evaluate the response of the treatment or progression of the disease which may be done by USG/CT/MRI. Skin elasticity and subcutaneous tissue thickness (Suprafascial and subfascial)may be assessed by the USG transducer to detect the progression of lymphedema [15–17].

Ultrasound evaluation of subcutaneous tissue thickness is a useful parameter to evaluate lymphedema and its response to treatment. These are measurements allow periodic evaluation of the response to therapy and serve the purpose of monitoring the progression of LMs and predicting prognosis [18, 19].

Thickening of all 3 components: cutaneous, epifascial, and subfascial with high-frequency USG (20 MHZ) is observed always to identify and classify lymphedema with fluid localization in various types of edema. Ultrasound is used for the diagnostic purpose as well as therapeutic monitoring.

11.5 Arterio-Venous Malformations (AVM): Key Points

AVMs are congenital anomalies comprising both arterial and venous systems. They are classified as truncular or extratruncular and may be associated with other CVMs such as VMs, LMs, and CMs or may be part of a generalized syndrome like the Parkes–Weber syndrome (PWS).

Duplex ultrasound is the first choice investigation amongst noninvasive modalities in clinical assessment and subsequent follow-up of AVMs either after intervention or after observation for a long time.

11.6 Arterial Malformations: Key Points

There are two variants for sciatic artery malformation. Either the sciatic artery coexists with normal iliac-femoral arteries or it may be accompanied and compensates for an aplasia of the iliac-femoral arteries. Both the conditions are easily identified by ultrasound. The symptoms manifest due to the compression of the sciatic nerve, distal embolization, and acute ischemia secondary to the thrombosis of the aneurysmal sac [20, 21]. The role of investigations should be appraisal of these finding apart from sciatic artery malformation.

11.7 Magnetic Resonance Imaging (MRI)

Almost all forms of vascular malformations need ultrasound evaluation for the assessment of the lesion initially as during the intervention or evolution phase but the investigation of choice in most vascular malformations remains MRI. Better spatial resolution/definition and a wider field of view give MRI always an edge over the ultrasound. The biggest advantage is the capability to visualize blood flow and characteristics of tissues without risks of ionizing radiation [22, 23]. However, both USG and MRI have the possibility of multiplanar acquisition (Fig. 11.4).

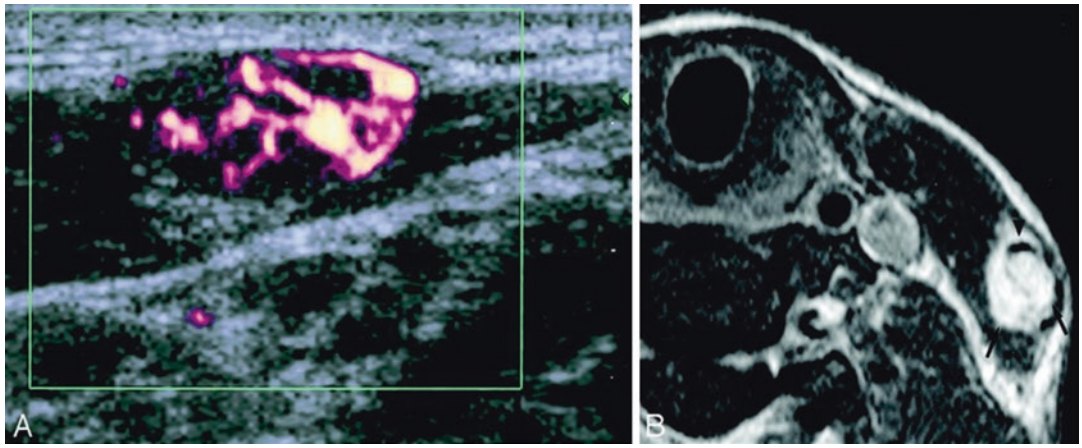


Fig. 11.4 Sonographic and MR images obtained in a vascular malformation of the left external jugular vein

Vascular malformations should be investigated with equipment of high power (at least 1.5 Tesla) to have better contrast and spatial resolution which identifies and detects even small anomalies [24]. Some of the drawbacks of MRI are that longer duration in the examination, noise above normal level, and claustrophobic feelings leading to fear and difficulty mostly in the examination for the children with the requirement of sedation and risks subsequently [22].

Each vascular anomaly has a unique MRI feature as summarized in Table 11.1 [25].

A typical Vascular malformation (VM) imaging protocol consists of spin echo (SE) or fast spin echo (FSE) in T1weighted sequences axial to the lesion generally with fat suppression in order to highlight the lesion. Later on images obtained after gadolinium contrast injection are useful to distinguish LMs and VMs which have similar images in the normal and angiographic acquisition. SE sequences can also identify signal voids representing arterial feeders [26].

T2-weighted images (FSE with fat suppression or in alternative short tau inversion recovery—STIR—images) in at least two planes are most sensitive and specific for identification of the extent and depth of the lesion because of a generally bright signal intensity lesion over a low signal intensity fat, muscle, and bone background. These sequences can also show the content of the malformation [22, 27].

The presence of signal voids on T2-weighted images is highly suggestive for hemosiderin, dystrophic calcification, or phleboliths which are typical findings for venous malformations [23].

Magnetic resonance angiography (MRA) techniques are complementary to the conventional MRI once definitive intervention is planned in vascular malformations and it is termed as contrast-enhanced MRA (CE-MRA) [28] which uses 3D T1-weighted sequences with fat suppression: the contrast medium (gadolinium chelates) is injected in a peripheral vein causing a shortening of T1 relaxation times [23].

CE-MRA can be done by a variety of techniques, but time-resolved 3DMR digital subtraction angiography is the Gold standard for evaluating vascular anomalies. In this technique, a serial acquisition of images of less than or equal to 10 second duration is performed in rapid succession. At least one acquisition will certainly coincide with the arterial phase and at least one will coincide with the venous phase of enhancement. Of course for optimal visualization, the temporal resolution must be maximized. Improvement of data processing techniques can generate 3D images every 2 seconds [23].

Multiplanar reconstructions, no use of ionizing radiation, non-invasive modality are definite advantages of CE-MRA over the conventional MR angiography. The drawbacks of CE-MRA are usually are identified that spatial resolution and the area of interest are influenced by a high

Table 11.1 MRI Imaging features of vascular anomalies

Vascular pathology	MRI Imaging features
Hemangioma of infancy (HOI)	In the proliferating phase appearance of a well-lobulated mass with low signal intensity on T1W images and high intensity in T2W images, presence of flow voids in SE T1W images, no perilesional edema, and early homogeneous enhancement Involuting phase: Fat replacement with high signal T1W images and decreased enhancement
Venous malformations (extratruncular)	Lobulated sometimes septated mass with low sig intensity in T1W images, high intensity in T2W images, flow voids in T2W fat saturation images (phleboliths), slow gradual enhancement in delay with contrast media
Lymphatic malformations (extratruncular)	The same characteristics of the venous malformations. No enhancement in microcystic malformations. Septal and rim enhancement in macrocystic malformations
Capillary	Skin thickness lesion
Arterio-venous malformations (extratruncular)	Enlarged feeding arteries and draining veins. Flow voids in T1W SE se-quences; early enhancement of arteries nidus and draining veins

time resolution selectivity is not associated to limit its role in selective catheterization [29].

In summary, MR imaging (MRI) is a major noninvasive test together with the Duplex ultrasonographic (DUS) evaluation. Better spatial resolution is the best parameter with MRI covering a wider field of examination which allows to highlight layer-wise different anatomic components decided by magnetic stimulation of the organs. The best evaluation tool for organ involvement in vascular malformation is definitely MRI.

11.7.1 Extratruncular Venous Malformations (VM)

MRI along with MR venography (MRV) are complete tools for evaluation of venous malformations. The Extension, type of the VM, feeding and draining vessels, adjoining soft tissue (muscle, fascia, fat), the vascular structures (arteries, veins), and nerve trunks can be identified easily. MRI and MRV are therefore, essential imaging modality to provide a highly accurate diagnosis before performing interventions on VMs [30].

MRI findings of the VMs including the typical appearance of VMs as a collection of serpentine structures and its relationships with adjacent tissue/structures were thoroughly described in the diagnostic section of the VM. They usually show low to intermediate signal in T1-weighted sequences and high contrast in FSE.

T2weighted or STIR sequences, where the vascular malformation is highlight from the surrounding fat (Fig. 11.5). In case of thrombosis or hemorrhage heterogeneous signals are seen in T1-weighted images. VM lesions may be localized or diffuse or have lobulated margins.

A slow filling of the malformation is visible with the use of contrast medium [28]. This characteristic of the VMs is important in the differentiation with the LMs and other cystic lesions which do NOT have any contrast enhancement after gadolinium injection.

The morphological features of VMs correlate with the success of the sclerotherapy [29]. Well-defined margins and dimensions less than 5 cm are predictive of good results after ethanol therapy.

11.7.2 Extratruncular Lymphatic Malformations (LM)

MRI findings in microcystic LMs are usually diffuse areas with low signal intensity with T1-weighted and high signal intensity in T2-weighted imaging sequences [29]. Small cysts in microcystic LMs are difficult to be individually identified on MRI and they are no flow lesions with complete avascularity or only mild enhancement.

On the other hand, the macrocystic LMs are easily identified for the presence of cysts and well-defined septa (Fig. 11.6). Low signal intensity on T1-weighted sequences and appear markedly hyperintense on T2weighted images

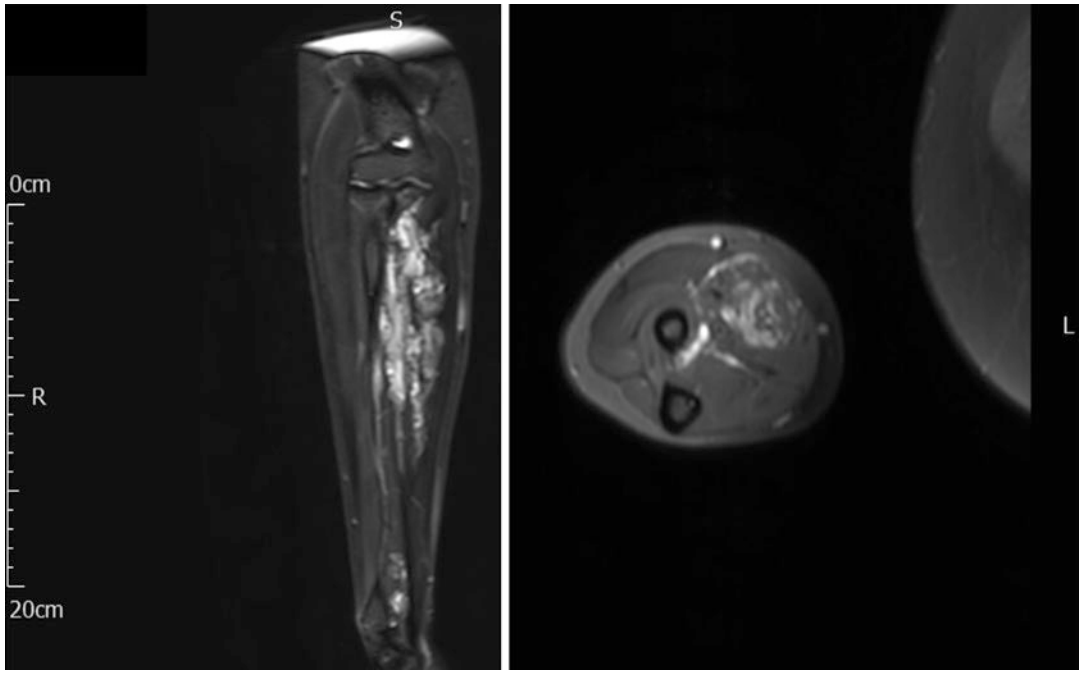


Fig. 11.5 MRI with Coronal STIR and Axial T1 weighted images of a low-flow venous malformation showing Typical high signal and enhancing venous spaces

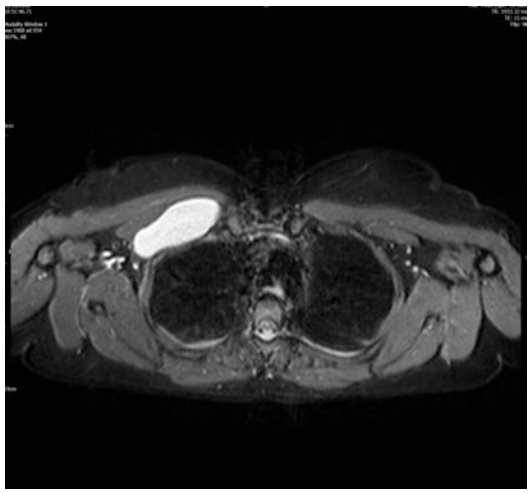


Fig. 11.6 Axial T2 weighted chest MRI with a large bright left side anterior chest wall macrocystic malformation

are characteristic features in macrocystic LMs. Fluid–fluid level within the cyst is identified, due to the presence of blood or proteins.

The septa and the walls of the cyst after injection of contrast present a Mild enhancement in the septa and the walls of the cysts after contrast injection which is never in cystic spaces. Mild enhancement in cystic spaces is finding with venous malformations. An enhancement of the cyst can be recognized after treatment sometimes or in the case of associated mixed malformations (LVM) [29].

11.7.3 Arteriovenous Malformations (AVM)

The blood vessels in AVMs cause Linear or rounded signal voids are identified as blood vessels in AVM in the T1weighted SE sequences which correlates with signal hyperintensity in the GRE sequences [23, 29]. Nidus is characterized by heterogeneous tangle of multiple empty signal in T1-weighted sequences in association with dysplastic veins, well identified in the T2-weighted sequences [27]. Thickened skin, increasing fat tissue, and reduced muscle mass are in associated findings with AVM. The AVM can affect Bone may be affected causing hypo-

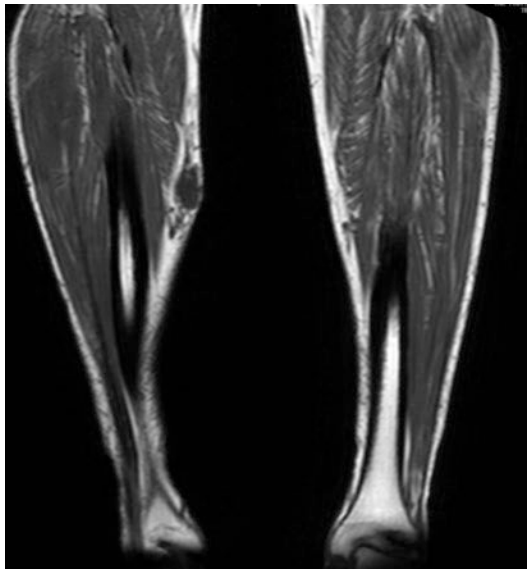


Fig. 11.7 MRI STIR both legs show arteriovenous malformation at the right leg medial side

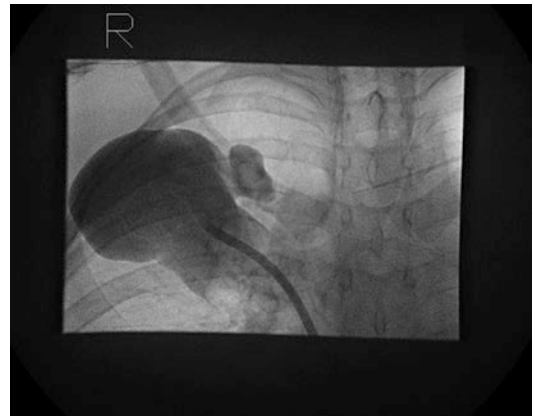


Fig. 11.8 Percutaneous sclerotherapy of a large right-side anterior chest wall lymphatic macrocystic malformation. Contrast injected under fluoroscopic guidance opacity macrocystic lymphatic space

plasia, cortical thinning and demineralization, or direct involvement of the bone which is identified by the presence of intraosseous high flow vessels [23, 27, 31].

Altered signals in surrounding tissue may be indicative of edema which can be detected with MRI examination (Fig. 11.7). The differential diagnosis between an AVM and a vascular tumor (rhabdomyosarcoma, hemangiopericytoma, angiosarcoma) can be very difficult and useful parameters in the diagnosis of AVM are the presence of fat within the lesion, muscle atrophy, and absence of surrounding edema [1].

CE-MRA is used to identify a dilation of arteries, dilatation of veins, early identification of the draining veins, detailed demarcation of vascular anatomy which is useful for the treatment or further work-up angiography [23].

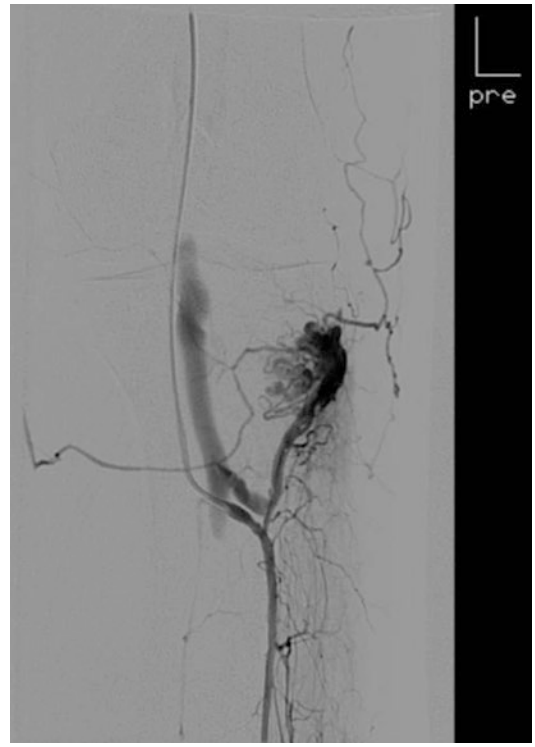


Fig. 11.9 Left knee arteriovenous malformation embolization and sclerotherapy

11.7.4 Follow-Up Studies

Treatment success with vascular malformation in follow-up studies may be identified with reduction in size or reduced flow. Response after percutaneous sclerotherapy (Fig. 11.8) or surgical excision (low-flow malformations), transarterial embolization (high flow malformations) are assessed with contrast injection of gadolinium (Fig. 11.9) always during follow-up studies which allows detection of the perfused area [32].

11.8 Computed Tomography (CT)

Preferred investigation after basic duplex scanning is MRI in vascular malformations but sometimes CT may be either a substitute or complementary to MRI in some selected cases. CT is an alternative investigation to MRI in those group of patients who are at high risk or with fragile health due to respiratory or cardiac as the images acquisition is very fast in CT as compared to MRI. Another situation where it is useful in patients who have contraindications to sedation with MRI and is preferable to MRI in imaging vascular anomalies of bowels and lungs [22].

Fewer artifacts are always with CT as compared to MRI in patients with embolization coils or metallic clips. Apart from less artifacts, CT better defines bone, calcifications, and phleboliths [27]. In bony involvement with high flow vascular malformations, CT may provide more information as compared to MRI.

The adverse effects are always more with CT and exposure to ionizing radiation and subsequent risk of malignancy especially for pediatric populations and risks increase more in vascular malformations due to the necessity of the use of contrast to visualize the vessels.

Venous Malformations (VMs) usually appear as hypodense or heterogeneous lesions which enhance slowly from the periphery after the injection of contrast [32].CT venography is an excellent tool for evaluation of obstructed, anomalous, atretic, absent veins along with and other anomalies of large veins in the chest, abdomen, or pelvis. Identifies the underlying pathology, confirming venous obstruction or extrinsic compression, delineating anatomic variations and the extent of venous thrombosis are best assessed with CT venogram [33, 34].

Low-attenuation masses occasionally with fluid–fluid levels and peripheral contrast enhancement of the wall are characteristic in lymphatic malformations (LMs) [32].

CECT of AVMs usually done, with bolus tracking technique (CT-angiography:CTA) to get an optimal study of arterial vessels, including enlarged feeding arteries and rapid shunting of contrast into enlarged draining veins without significant intervening tissue enhancement which is usual within a normal capillary network. Best use of Contrast-enhanced CT is possible with AVMs which is significantly more informative as compared to other vascular malformations because it provides a distinct three-dimensional data set for accurate mapping and measurement of arterial, nidal, and venous structures and assessment of flow patterns for interventional radiologic or surgical planning which is possible especially due to the many post-processing options [35].

CT with intravenous contrast enhancement has been used for the differential diagnosis of hemangiomas and VMs [36].

Standard MRI is not a good technique for precisely demonstrating the nidus or arteriovenous connection. Instead, CTA provides much better anatomical information, sometimes showing the arterial and venous anatomy in excellent detail, but is inferior in all aspects to the newer technique of CEMRI [1].

Even considering that CTA may give more precise anatomical detail than MRI, particularly in small blood vessels, the benefits of clinically justified CT examinations should always outweigh the risks for an individual child, and referral to a center that performs CE-MRI should be considered as well.

MRI should remain as the option of choice in the diagnosis of high flow vascular anomalies for this special group. Only when dealing with a specific AVM in a critical area difficult to treat, CT is indicated, though extremely rare [1].

CT scan is a useful test in association with the contrast medium providing excellent spatial and temporal resolution. Thoracic and visceral malformations as well as AVM with bone involvement are assessed better with contrast-enhanced CT.

11.8.1 Radiography

Plain X-ray films are of limited use as low soft tissue contrast resolution is not much helpful. It is most useful in demonstrating soft tissue overgrowth, bony hypertrophy, bony erosion, periosteal reaction, pathological fracture, limb length discrepancy, and phleboliths. The presence of phleboliths in soft tissues is suggestive of a low-flow venous malformation (Fig. 11.10).

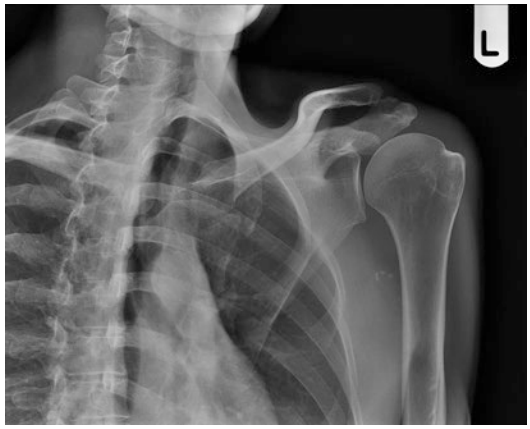


Fig. 11.10 Few tiny calcification foci (Phlebolith) in soft tissue at the level of proximal shaft of humerus

Scanograms are long bone radiographs that provide accurate measurement of the long bone length of the upper and lower limbs. Scanograms are needed to assess any bone length discrepancy between the limbs. This document would become objective criteria for further management [37].

Conventional radiologic techniques are addressed to discover bone involvement in CVMs. Bones may be elongated, shortened, deformed, thickened, or thinned because of osteolysis [22]. The pathological cause is related to ischemia of the osteoblasts representing a growth stimulation or to compression of the bone by the surrounding structures or vein and lymph stasis.

Calcification in the soft tissues is a hallmark of VMs. Multiple enchondromas are typical of Maffucci syndrome and they have the tendency to progress to malignancy.

Plain X-rays are an essential test in detecting basic bone pathology including lengthening, shortening, enchondromas, and vanishing bone syndrome. These images are also useful in detecting calcifications (phleboliths) in soft tissues which is diagnostic feature of VMs.

11.9 Invasive Diagnostic Evaluation

- Venography/phlebography (ascending/descending/segmental)
- Arteriography (standard/segmental)
- Percutaneous direct puncture angiography: arteriography, phlebography, varicography, lymphography

"Invasive" tests are rarely required needed to establish the diagnosis of the Vascular Malformations as Non- invasive tests are sufficient enough to establish the diagnosis most of the time as invasive tests should be deferred until intervention is planned. The role of invasive tests is limited as it is required for treatment planning either surgical or endovascular. However, invasive tests may be required for diagnosis when non- to minimally invasive tests (e.g., CT and/or MRI) fail to confirm the diagnosis or to delineate important diagnostic details which are important for options of treatment [10].

Ascending phlebography combined with intravascular ultrasound (IVUS) for identification of lesion and proper therapeutic planning in case like truncular lesions along iliac vein is ideal tool studies is essential for proper management. The role of descending phlebography is an integral component for the assessment of deep venous reflux along the pelvic veins and/or sciatic veins. Any embolotherapy intervention must be preceded by phlebography for better planning and identification of the lesion for therapeutic intervention.

Direct puncture phlebography is also very useful to identify a large efferent vein of extratruncular lesions [38, 39]. These veins can be treated in advance to allow more effective therapy with reduced risk of recurrence, with subsequent embolotherapy or sclerotherapy [1, 25].

Angiography should be reserved only in AVM as a road map to further define the lesion and plan proper treatment. To minimize radiation exposure, these techniques are usually performed at the time of treatment in young patients [40].

These studies include:

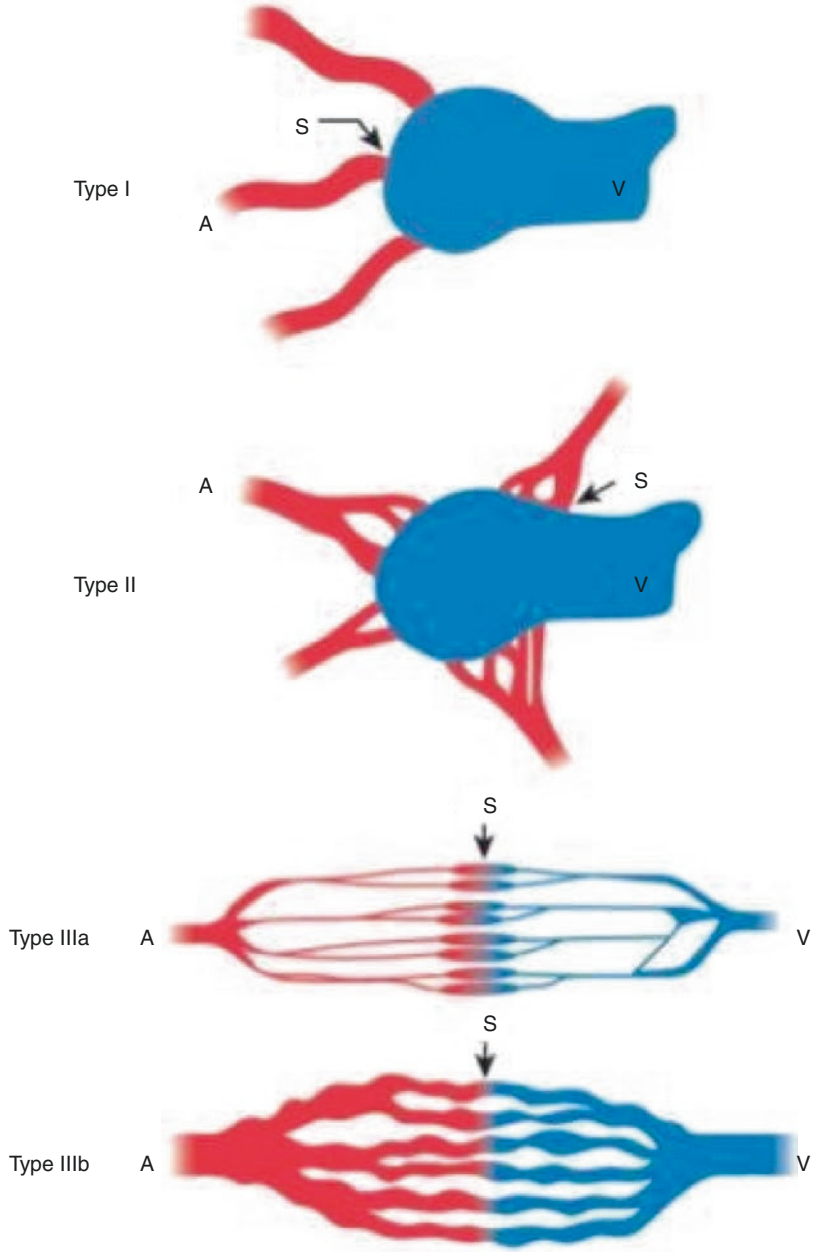
- Selective and superselective arteriography
- Percutaneous direct puncture phlebography

Therefore, once the intervention is decided, complete pretherapeutic mapping of the lesion is

essential including the angiographic classification of extratruncular VMs (Table 11.2) and also AVMs (Flow Diagram 1) proposed by Puig and YS Do et al., respectively [41, 42]. These classifications have a great importance as predictive measurement for the results of intravascular therapy.

Table 11.2 Angiographic classification of Venous Malformation [41]

Description	
Type 1	isolated malformation without peripheral drainage
Type 2	malformation that drains into normal veins
Type 3	malformation that drains into dysplastic veins
Type 4	malformation that represents a ectasia



Flow Diagram 1. Arteriographic classification of AV Malformation [42]. Type I (arteriovenous fistulae): at most three separate arteries shunted to a single draining vein. Type II (arteriovenous fistulae): multiple arterioles shunted into a single draining vein. Type III (arteriovenous fistulae): multiple shunts between the arterioles and venules

Phlebography

Hemodynamic characteristics and classification of vascular malformation are best assessed with phlebography as anatomy is best derived along with communication pattern and draining venous system Based on the appearance of the VMs and the draining venous system during phlebography all VMs can be classified into four distinct groups: Type I (isolated VMs without phlebographically appreciable venous drainage), Type II and Type III VMs (demonstrate normal sized and enlarged venous drainage, respectively) and Type IV VMs (characterized by essentially ecstatic dysplastic veins) [41, 43].

From a diagnostic work-up, phlebographic evaluation of patency and anatomic variations of the deep venous system deserves special consideration in addition to phlebographic classification of the VM. Although above mentioned phlebographic classification does not provide information regarding the location of the VMs or the involvement of surrounding anatomical structures it provides useful data for treatment planning, especially when the sclerotherapy is considered as a treatment option [1].

Ascending phlebography is of limited use only for the diagnosis of truncular venous disease and in particular of superficial veins and hypoplasia or aplasia of deep veins according to the noninvasive investigations [38, 39]. Technical skills are required to avoid incorrect results of phlebography, as preferred abnormal outflows may sometimes simulate absence or main vein stenosis.

The main advantage of this procedure is that the imaging can be performed in orthostatism [25]. Descending phlebography is indicated in pelvic, sciatic, and visceral malformations. Direct puncture venography is related to the treatment of extratruncular VM lesions. With this procedure, it is possible to visualize the outflow drainage of the malformation and it is possible to distinguish four types according to the drainage veins.

Direct puncture phlebography is used for the evaluation of the venous outflow of the lesion. It helps in understanding the success probability of a vascular surgical procedure or sclerotherapy. Retrograde phlebography is useful to evaluate deep venous incompetence in the lower limbs, visceral and pelvic malformations.

Arteriography

Arteriography is now almost obsolete with the availability of MRI and CT scans for the management of the vascular malformations in general but it still remains as the gold standard for the precise assessment for the AVMs and warranted for the planning of the treatment of an AVM which were already studied with non-invasive diagnostic tools.

It is necessary to have panoramic and superselective pictures in order to highlight the feeding arteries to lead to the nidus. It is possible to adopt an arteriographic classification of AV shunts in order to guide the therapy as mentioned in detail above [42].

Atreriography is an invasive investigation and used only for the patients who need a therapy and it should be performed at the centers which deliver the therapy.

Lymphography

In evaluations of LMs, Invasive tests are rarely required for the diagnosis but occasionally needed for differential diagnosis as well as sometimes for confirmation of the diagnosis [43]. The usual protocol is to defer the invasive tests. Direct puncture percutaneous lymphangiography can be generally deferred to later stages if there is a need for refining the diagnosis or if surgical or other invasive therapeutic measures are considered. It is reserved for road-mapping in subsequent therapy if needed.

Conventional oil contrast lymphangiography when combined with CT scan, is very informative in selected patients with chylous dysplasia and gravitational reflux disorders in order to define more clearly the extension of the pathologic alterations and sites of lymphatic and chylous leakage. These are the only diagnostic investigations that can clearly demonstrate pathologies of chylous vessels, chylous cyst, and thoracic duct in cases of chylothorax, chylous ascites, protein-losing enteropathy, etc. [19, 44, 45].

Lymphography has been substituted by lymphoscintigraphy for the diagnosis of lymphedema. There is a revival in the use of lymphography in case of lymphoceles, and pathology of chylous reflux. In this case, a direct puncture of inguinal nodes is made under ultrasound and lipiodol infused. The procedure causes the inflammation of the lymphatic pathways and may be curative [46, 47].

11.10 Nuclear Medicine Evaluation

11.10.1 Whole Body Blood Pool Scintigraphy (WBBPS)

The presence of a vascular malformation is detected by WBBPS using Tc99. The advantage lies with a single examination detecting the presence of any vascular malformation in the whole body. The main strength associated with WBBPS, is the ability to investigate all anatomic structures in one examination. It gives Some quantitative data on the blood trapping of the lesion can be derived easily which calculates the possibility to assess the results of treatment [48, 49].

WBBPS is an screening test used sometimes in multiple VM lesions which are scattered in the whole body. It allows qualitative and quantitative evaluation of the VM lesion especially during multisession sclerotherapy as a cost-effective measure. It is an excellent tool for routine follow-up and the evaluation of therapy to assess the progress of treatment and the natural course of the VM lesion with some numerical values. It can exclude the LM where the absence of an abnormal blood pool over the lymphatic lesion is the typical finding [1].

WBBPS is also an excellent optional test for the AVM evaluation as well. But it is rather more useful for the screening of hidden CVM lesions throughout the body and for a qualitative analysis of the AVM lesion along the course of the multisession therapy as a cost-effective measure. It is an excellent tool for the routine follow-up on the progress of treatment and its natural course as well when TLPS is not feasible/available [50, 51].

Whole body blood pool scintigraphy as a very useful tool to detect the presence of a vascular malformation throughout the body.

11.10.2 Transarterial Lung Perfusion Scintigraphy (TLPS)

An essential examination is scintigraphy which is necessary for the diagnosis of AVM and CVM in general but it remains an option as a secondary investigation only in few selected cases. TLPS has a unique role in determining the degree of AV shunting by the AVM lesion within an extremity [52, 53].

TLPS has a special role to detect and assess a micro-AV shunting lesion, which is often difficult with conventional techniques. Micro-AVMs frequently exist in the combined form of CVM, the hemolymphatic malformation (HLM), and its delayed or overlooked diagnosis with subsequent progress beyond the optimum time for the interception can be avoided with TLPS alone [52–54].

TLPS allows not only to quantify the AV shunt present in a malformation but also provides quantitative measurement of the shunting status during therapy [55]. TLPS may replace the substantial role of traditional arteriography as a follow-up assessment tool for extremity AVMs. TLPS is not indicated for evaluation of the VM lesion but its major function is to rule out the presence of a combined AVM lesions [54]. Transarterial lung perfusion scintigraphy should be used to quantify the AV shunt in an AVM only in indicated cases.

11.10.3 Radionuclide Lymphoscintigraphy (LSG)

LSG is basically a physiological and functional study which complements the anatomical information provided by lymphangiography. There are no standardizations nor is there a gold standard as of yet [13, 19]. It is performed with injection of 99mTclabeled human serum albumin or 99mTc-labeled Sulphur Colloid subcutaneously

into the first and second webspace of the toes or fingers, is the test of choice to confirm or exclude lymph vessel pathology as the cause of chronic limb swelling [13, 19].

Movement of the colloid from the injection site, the transition time to the knee, groins or axilla, absence or presence of major lymphatic collectors, number and size of vessels and nodes (e.g., popliteal nodes), the presence of collaterals and reflux, symmetric activity with the opposite side are recorded and used for interpretation. Semi-quantitative assessment has been reported, and most recently, the technique of quantitative assessment of transit time from the foot to the knee was also validated [56, 57].

LSG represents the main examination to evaluate the lymph dynamics of the limbs. This will be recorded in rest, after exercise, and 1 h of daily activity. With this examination, it is possible to detect the presence of deep and superficial lymphatic vessels and the presence or absence of reflux. In patients with genital and abdominal lymph leakage, there is an indication for SPECT examination to visualize the intraabdominal lymph node status [25].

LSG is essential to rule out lymphatic dysfunction especially due to the presence of a truncular LM known as primary lymphedema, which often exists with the VM lesion (e.g., KTS) [58, 59].

LSG remains the gold standard for lymphatic function evaluation since the LSG is the only test that can clearly indicate lymphatic function. Radionuclide lymphoscintigraphic findings provide the proper clinical and/or laboratory staging that may be essential for proper clinical management.

LSG, along with clinical evaluation, is the most essential component for the diagnosis of chronic lymphedema.

LSG is extremely useful for identifying the specific lymphatic abnormality and has largely replaced conventional oil contrast lymphography for visualizing the lymphatic network. LSG can easily be repeated with minimal risk. Data and images obtained from the study identify lymphatic (dys)function, based on visualization of lymphatics, lymph nodes, and dermal backflow as well as semi-quantitative data on radiotracer (lymph) transport.

However, the LSG has not been standardized with regard to the various radiotracers and radioactivity doses, different injection volumes, intracutaneous vs. subcutaneous injection site, epi-or subfascial injection, number of injections, different protocols of passive and active physical activity, varying imaging times, static and/or dynamic techniques.

Lymphoscintigraphy is the most essential non-invasive test for a morphodynamic evaluation of the lymphatic circulation.

11.11 Laboratory Tests

Coagulation disorders usually associated with high frequency in patients with extensive VMs and may result in potentially severe thromboembolic events and hemorrhagic complications [1]. Extensive VMs usually leads to “localized intravascular coagulopathy” (LIC). LIC results due to stagnant flow in extratruncular lesions leading to a cycle of ongoing intravascular thrombosis and fibrinolysis. Secondary hypofibrinogenemia is the end point spontaneous hemorrhage.

Currently, there are no evidence based guidelines to advocate screening for coagulopathy in patients with potentially lifethreatening VMs. It is important to follow an accurate diagnostic algorithm for coagulopathies associated with especially extensive VMs involving large surface areas, muscle involvement, and/or palpable phleboliths [1].

Assessment of the coagulation profile and D-dimer levels is indicated in patients with extensive VMs. D-dimer (a degradation product of crosslinked fibrin) measured with rapid enzyme-linked fluorescent immunoassay is being increasingly utilized in the assessment of VM patients and is the biochemical gold standard for ruling out an episode of thrombophlebitis or thromboembolic events.

D-dimer can detect a sign of consumptive coagulopathy which is common among VMs [60, 61].

Elevated D-dimer among the symptomatic VMs has a unique value for the clinical assessment of the severity of the VM lesions although D-dimer in general is highly non-specific. D-dimer levels may also assist in the diagnosis of occult lesions and help differentiate GVMs and LMs (normal D-dimer levels) from other multifocal venous lesions.[237] Therefore, in addition to imaging studies, plasma Ddimer representing a direct measurement of endogenous fibrinolysis as a biological marker should be evaluated in the diagnosis and followup of VMs.

Patients with *extensive* VMs or *high-risk* lesions, in particular, should undergo the following laboratory tests

- Full blood count including hemoglobin levels and platelet count
- Ddimer-quantitative assay
- Fibrinogen
- PT, APTT
- Thrombophilia screening

D-dimer measurements to detect elevated values linked to the presence of VMs, platelet count, and fibrinogen levels in Kasabach Merritt syndrome often associated with kaposiform hemangioendotheliomas.

11.11.1 Histology

Biopsy should be reserved to make an accurate diagnosis and is mostly required when the lesion is suspected to be a tumor. Biopsy may be required to differentiate between AVMs, NICH, and vascular sarcomas. Histologic differentiation between HOI and congenital hemangiomas may be required and can be facilitated by GLUT1 staining of HOI which persists also after regression. Biopsy may also be required to differentiate between GVM and BRBNS.

Recently, immunohistochemistry has been used in the study of hemangiomas and supports a new classification of the pediatric liver vascular tumors based on the expression of GLUT1 as a substitution of the old and confusing term of hepatic infantile hemangioendothelioma.

GLUT1 positive expression is usually demonstrated in multifocal, and diffuse hepatic infantile hemangioma which shares clinical and morphological features with cutaneous infantile hemangioma. Diffuse neonatal hemangiomatosis is a disorder characterized by multiple cutaneous and hepatic hemangiomas [62].

Therefore, timely identification of GLUT-1 expression is crucial for children with hepatic hemangiomas in view of improved management before reaching the liver transplantation. In the last 5 years, propranolol has dramatically changed the scope of children with hepatic hemangiomas. Prognosis is currently considered as favorable and those previously considered as unfortunate patients are not any more candidates for liver transplantation.

Biopsy should be recommended only for unclear cases.

11.11.2 Endoscopic Evaluation

Endoscopic examinations are recommended when vascular anomalies are suspected to involve intracavity organs. This is usually performed when investigating the causes of occult bleeding.

CVMs located on the face and neck often require early pharyngolaryngotracheoscopy as the possible associated mucosal involvement may result in bleeding, infection, or respiratory complications. Conventional imaging techniques may not be precise enough to detect such lesions. Endoscopic identification and destruction of the lesion may be achieved during the same session.

Malformations located in the pelvic cavity and lower extremities often need proctosigmoidoscopy, urethrocystoscopy, and/or vaginoscopy (colposcopy) for early detection before bleeding occurs. This is especially true in patients with KTS which accompanies a high incidence of gastrointestinal and genitourinary involvement.

Arthroscopy is indicated to assess lesions involving the knee as small lesions are frequently not detected by conventional imaging techniques. Accurate assessment is required for subsequent laser coagulation.

Patients with BRBNS need regular esophago-gastro-duodenoscopy and complete colonoscopy due to the high risk of gastrointestinal mucosal involvement that can cause severe bleeding.

11.11.3 Genetic Testing and Family Screening

Germline and somatic mutations have been identified in a few vascular anomalies. Germline mutations were identified when practitioners observed a familial occurrence of some vascular lesions, and blood samples from these individuals enabled researchers to identify these mutations. Sporadic syndromes are thought to occur due to the mosaic distribution of somatic mutations that are detected from studies of affected tissue [63–67].

However, certain vascular anomalies occur with variable penetrance, such that parents of the proband patient may harbor a genetic mutation without overt expression of the disorder (e.g., GVM). If these parents are interested in further offspring (and the genetic mutation has been identified), prenatal genetic testing can be offered.

Options include chorionic villus sampling, amniocentesis, or pre-implantation genetic testing with in vitro fertilization of an unaffected embryo. Identification of the PTEN mutation requires counseling regarding the necessity for early and consistent surveillance for early detection of malignancies. Additionally, affected patients can be educated about their chances of having affected offspring.

Identification of somatic mutations may have implications for new therapies. In many cases, discussion with a specialist in human genetics and/or genetic counselor is recommended. In the USA, many insurance plans require prior authorization for this testing, which may be costly. Some research laboratories are interested in patient/family blood and/or tissue samples for genetic studies.

11.11.4 FollowUp Assessment

Follow-up is essential to evaluate the natural evolution of the disease even without treatment or with treatment in terms of pathology and/or the therapy results. The follow-up assessment tools are non-invasive investigations usually (MRI and ultrasound). A transient increase in size after endovascular intervention is usually observed most of the times. Using WBBPS, scattered or multiple vascular malformations can be usually identified during follow-up .

Follow-up evaluation to evaluate the natural evolution of the pathology and/or the therapy results. The follow-up shall be based on non-invasive investigations (MRI and ultrasound) mostly and sometimes invasive investigation like WBBPS.

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