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Clinical and sonographic features of pediatric soft-tissue vascular anomalies part 2: vascular malformations

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Abstract Vascular malformations are a heterogeneous group of entities, many of which present in the pediatric age group. Sonography plays a major role in the management of children with these vascular anomalies by providing information that helps in diagnosing them, in assessing lesion extent and complications, and in monitoring response to therapy. The interpretation of sonographic findings requires correlation with clinical findings, some of which can be easily obtained at the time of scanning. This has to be combined with the use of appropriate nomenclature and the most updated classification in order to categorize these patients into the appropriate management pathway. Some vascular malformations are part of combined vascular anomalies or are associated with syndromes that include other disorders, frequently limb overgrowth, and these are now being reclassified based on their underlying genetic mutation. Sonography has limitations in the evaluation of some vascular malformations and in these cases MR imaging might be considered the imaging modality of choice, particularly for lesions that are large, that involve multiple compartments or are associated with other soft-tissue and bone abnormalities. In this article, which is part 2 of a two-part series, the authors review the most relevant clinical and sonographic features of arteriovenous, capillary, venous and lymphatic malformations as well as vascular malformations that are part of more complex conditions or associated with syndromes, including Parkes–Weber syndrome, phosphatase and tensin homologue (*PTEN*) hamartoma tumor syndromes, Klippel–Trénaunay syndrome, CLOVES (congenital lipomatous overgrowth, vascular malformations, epidermal nevi and skeletal anomalies) syndrome, fibro-adipose vascular anomaly and Proteus syndrome.

Keywords Children · Doppler · Overgrowth · Soft-tissue masses · Ultrasound · Vascular malformation

Introduction

As mentioned in the part 1 of this series, vascular malformation is one of the two broad categories in which vascular anomalies are divided in the classification proposed by the International Society for the Study of Vascular Anomalies (ISSVA) [1] (Table 1).

Sonography plays a major role in the evaluation of vascular malformations by providing valuable information that helps in diagnosing, in assessing lesion extent and complications and in monitoring response to therapy. One must reiterate that the interpretation of the sonographic findings has to be correlated with the clinical findings. When the clinical information has not been provided by the referring clinician, the sonographer or the radiologist has the opportunity to get valuable clues by asking a few basic questions and observing the lesion just before starting the US examination (see part 1 of this series). The final interpretation should not only discuss the sonographic findings but should also make use of appropriate nomenclature referring to the most updated classification because this information is used to categorize these patients into the appropriate management pathway.

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Table 1 Vascular malformations based on the International Society for the Study of Vascular Anomalies (ISSVA) classification [1]

Vascular malformations	
Simple	Arteriovenous
	Capillary
	Venous
	Lymphatic
Combined	(See text)
Of major named vessels	(See text)
Associated with other anomalies	*RASA1* gene mutation
	Parkes–Weber syndrome
	PTEN gene mutation
	Bannayan–Riley–Ruvalcaba syndrome
	Cowden syndrome
	PIK3CA gene mutation
	Klippel–Trénaunay syndrome
	CLOVES syndrome
	Fibro-adipose vascular anomaly (FAVA)*
	AKT1 gene mutation
	Proteus syndrome

CLOVES congenital lipomatous overgrowth, vascular malformations, epidermal nevi and skeletal anomalies, *PIK3CA* phosphatidylinositol-4, 5-biphospate 3-kinase catalytic subunit alpha, *PTEN* phosphatase and tensin homologue

*Not included in ISSVA classification

It is important to remember that sonography has limitations and might not be useful in accurately assessing the extent of larger and deeper lesions, in detecting flow in low-flow lesions and in assessing associated soft-tissue and bone abnormalities. In these situations MR imaging is a better option.

In part 2 of this series, we review the most relevant clinical and sonographic features of simple vascular malformations. These are summarized in Table 2. We also review some complex combined vascular malformations, which are often associated with syndromes, and we have categorized them based on their genetic origin.

Vascular malformations

In the 2014 revision of the ISSVA classification, vascular malformations were subdivided into four categories: simple, combined, of a major vessel, and associated with other anomalies [1] (Table 1). The simple vascular malformations were further categorized based on the type of vessel affected (arteriovenous, capillary, venous or lymphatic malformations). Combined malformations are those with two or more types of vascular malformation forming a lesion. Malformation of a major vessel includes anomalies of origin, course, number, length, diameter, valves, communication (arteriovenous fistula) and persistence of an embryonic vessel. Vascular malformations can be associated with multiple syndromes,

and in these conditions they are one of several presenting anomalies.

Vascular malformations are composed of abnormal vessels and show cellular turnover without proliferation or cellular hyperplasia [2, 3]. They are congenital but many vascular malformations are not evident at birth and manifest in infancy or even at a later age. They grow commensurately with the child although the growth can be stimulated by hormonal influence during puberty or pregnancy, trauma, clotting or can be idiopathic [2]. Regression is not expected to occur.

Arteriovenous malformation

Arteriovenous malformations represent anomalous connections between arteries and veins formed by a complex network of primitive vessels and with partial or complete absence of normal intervening capillaries [4]. Arteriovenous malformations are frequently in the differential diagnosis of high-flow lesions, although they are overall less common than many high-flow tumors. The clinical progression of arteriovenous malformations along with their severity is graded using the Schobinger classification, in which stage I represents a quiescent lesion, more often seen in young children. In stage II, the lesion has expanded and become warmer, with a palpable thrill. In stage III, there are signs of destruction with ulcers, hemorrhage or bone lytic lesions. Stage IV reflects the development of heart failure in a stage III patient [4]. One of the characteristic presentations at the time of imaging is growth and pain in a longstanding lesion, which is owed to its upstaging in the Schobinger classification, most commonly near times of puberty or pregnancy, and it is thought to be secondary to hormonal influences [5]. These patients commonly present with ischemic symptoms from arteriovenous shunting, bleeding and ulceration (Fig. 1). Precautions should be taken when scanning these lesions because they can be extremely fragile and a large amount of blood can be quickly lost. A US division plan for this, including a hemostasis kit, can be extremely beneficial. A hemostasis kit should at a minimum include one of the many commercially available hemostasis pads, 4″ × 4″ cotton gauze, a large occlusive adherent dressing, gloves and an elastic-type tape or self-adherent wrap for creating a pressure dressing if needed. A combination of endovascular embolization and surgical resection is the mainstay of treatment for arteriovenous malformations today.

On sonography, arteriovenous malformations are characterized by the presence of a conglomerate of tortuous vessels, which are often visible on gray-scale imaging, typically without a discrete soft-tissue mass [6–9] (Fig. 2). Sonography can be used to grossly estimate the size of the lesion and determine its complexity by assessing the number of inflow and outflow vessels and its association with adjacent structures [9]. Arteriovenous malformations can involve multiple soft-

Table 2 Clinical features and sonographic findings in vascular malformations

Vascular malformation	Clinical features	Sonographic findings
Arteriovenous	Schobinger stage I: quiescent, might mimic capillary malformation Schobinger stage II: red, warm plaque or mass with palpable thrill Schobinger stage III: ulcers, hemorrhage, lytic bone lesions Schobinger stage IV: stage III + heart failure	Conglomerate of tortuous vessels without discrete mass that can involve multiple soft-tissue planes High vascular density on color Doppler High velocities, low resistance and spectral broadening in arteries on spectral Doppler Pulsatile venous flow on spectral Doppler
Capillary	Well-defined port wine stain, usually segmental and unilateral	Often not visible or focal thickening of skin and subcutaneous soft tissues Low to moderate vascular density on color Doppler
Venous	Ectatic superficial veins, purple venous blebs or blue hue to involved skin If deep, might present as lump with normal overlying skin Enlarge when dependent or with exertion Pain is common	Variable appearance (spongiform, multicystic, uncommon as dilated tubular channels) Usually heterogeneous, mostly hypoechoic Intralesional phleboliths (calcifications) may be present Localized or involving multiple soft-tissue planes Low vascular density on color Doppler Venous flow, sometimes not detectable on Doppler
Lymphatic		
Macrocystic	Commonly in neck, axilla, groin and chest wall Often large, compressible or non-compressible, translucent, with normal or blue hue to skin Rapid enlargement with ecchymotic lesions from hemorrhage	Multicystic with thin septa Variable echogenicity of cystic contents, sometimes with fluid-fluid levels, especially if complicated with hemorrhage No flow or low vascular density on color Doppler, confined to septa
Microcystic	Commonly in axilla, shoulders, neck, proximal limbs Variable size Characteristic cutaneous vesicles with clear fluid or blood	Ill-defined and hyperechoic, containing scattered cysts <1–2 cm Sometimes no visible cysts No flow or low vascular density on color Doppler

tissue planes and adjacent bone [10]. Color Doppler interrogation reveals the characteristic high flow of these lesions by showing high vascular density with multidirectional flow.
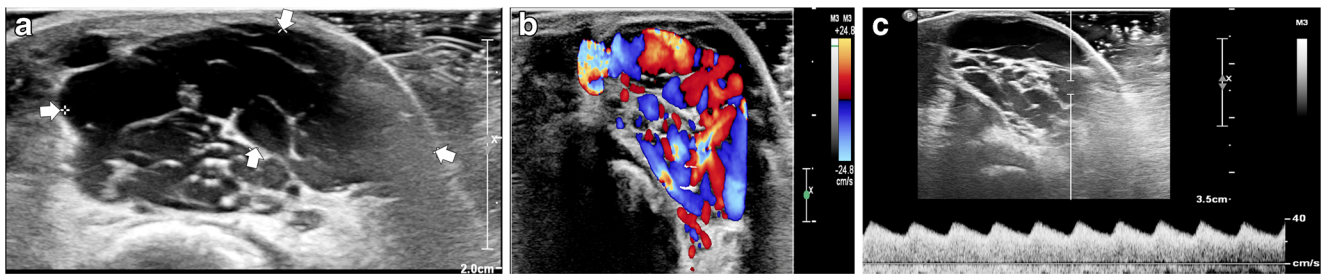

Fig. 1 Arteriovenous malformation with cutaneous ulceration (Schobinger stage III) in a 13-year-old girl who presented with rapid growth of longstanding pulsatile lesion in the face and upper neck requiring multiple transfusions. The malformation was successfully treated with endovascular embolization and surgical resection. (Parental consent was obtained for publication of this clinical photograph)

Spectral Doppler analysis shows high velocities, low resistance and spectral broadening in the arteries, which is more evident when compared with normal arteries in the adjacent soft tissues not involved by the malformation or in the contralateral side. Spectral Doppler analysis of the venous component shows pulsatile flow with relatively high velocities [6–9, 11–13] (Fig. 2). Spectral Doppler sonography can also be used to monitor response to interventional radiologic treatment [9].

In the series of Paltiel et al. [6], 43% of arteriovenous malformations had no gray-scale imaging abnormality and were only recognized using color Doppler sonography. Although this could be in part from lower resolution of older equipment, it still reinforces the value of using color Doppler sonography in the evaluation of suspected vascular anomalies.

Dubois et al. [11] reported three cases of arteriovenous malformation that presented on sonography with a small soft-tissue mass, in contrast to the classic description of lack of a discrete mass in this type of vascular anomaly. These cases can be difficult to differentiate from hemangiomas. This unusual sonographic pattern might be related to recent descriptions of a relatively high frequency of atypical findings of soft-tissue arteriovenous malformations on MR imaging, including 43% presenting with a discrete soft-tissue mass [14].

Fig. 2 Arteriovenous malformation (Schobinger stage II) in a 7-year-old girl who presented with persistent swelling in the left ankle for several months. **a** Transverse sonogram shows a subcutaneous mass composed of a tangle of prominent vessels (*arrows*). **b** Transverse color Doppler sonogram confirms the high vascular density of the mass. **c** Spectral Doppler analysis shows typical high-velocity arterial flow with a low-resistance pattern reflecting the abnormal arteriovenous communication

Fatty tissue is frequently seen surrounding arteriovenous malformations because of fibro-fatty proliferation [12]. However, this should be differentiated from the intramuscular fast-flow vascular anomalies seen in children with phosphatase and tensin homologue (*PTEN*) gene mutations, which are now referred to as *PTEN* hamartoma of soft tissue. In these hamartomas there is substantial amount of intralesional fat, which appears as hyperechoic tissue admixed with large vessels [15] (see section on *PTEN* hamartoma tumor syndromes).
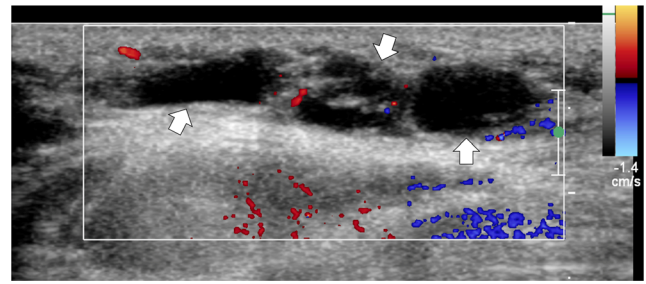

Fig. 3 Clinical photograph of venous malformations in a 15-year-old boy who presented with soft compressible masses (*arrows*) and diffuse purple skin discoloration in the upper extremity. The masses engorged when the arm was placed down and decreased in size when the arm was elevated. There was also skin discoloration in the right chest wall. These findings are all consistent with venous malformation

Capillary malformation

Several types of lesions are listed in the category of capillary malformations, including the port wine stain, a relatively common cutaneous or mucosal lesion seen in 0.3% of newborns [2]. This often presents as a well-demarcated red or pink macule in any area of the body, usually with a segmental distribution. Capillary malformations are not usually clinically significant in and of themselves, with the exception of significant cosmetic concerns, but these can be important because of their association with a host of other disorders, such as Sturge-Weber syndrome, the newly described diffuse capillary malformation with overgrowth [16] and several other entities that are discussed separately in this article. The treatment approach for capillary malformation typically involves pulsed-dye laser in addition to the specific treatment of the associated underlying vascular anomalies.

With the usual transducers, capillary malformations are often not visible or only manifest as focal thickening of the skin and subcutaneous soft tissues, which is easier to recognize when comparing with the normal contralateral side [6]. With dedicated sonographic equipment to evaluate the skin, including the use of 20-MHz transducers, capillary malformations can appear as superficial hypoechoic areas that vary in depth from 0.2 mm to 3.7 mm with a mean maximum depth of 1.0 mm [17]. However even with the use of this type of equipment, 18% of capillary malformations are not recognized [17]. Color Doppler sonography might reveal slightly increased vascular density when compared with the adjacent normal dermis [18], likely reflecting progressive dilatation of ectatic capillary channels [8].

Venous malformation

Venous malformations are the most common vascular malformation, with a prevalence of 1% in the general population [19]. They present clinically with dysplastic ectatic superficial veins or, more frequently, with a soft-tissue mass that can be associated with a bluish discoloration of the overlying skin if superficial in location (Fig. 3). They are usually very soft and

Fig. 4 Venous malformation in a 5-year-old girl who presented with growing purple blebs of the tongue and left face (*arrows*) and pain. These venous blebs are consistent with venous malformation. The girl was successfully treated with image-guided sodium tetradecyl sulfate sclerotherapy. (Parental consent was obtained for publication of this clinical photograph)

Fig. 6 Venous malformation in a 3-year-old boy who presented with a mass in the left posterior chest wall. Color Doppler sonogram shows a subcutaneous lesion composed of multiple small irregular anechoic spaces (*arrows*), some slightly tubular and others more round in shape, without internal flow. Flow only appears in the soft tissues adjacent to the presumed vascular spaces. The sonographic appearance of the lesion can be interpreted as a lymphatic malformation, but subsequent MR imaging (not shown) revealed enhancement of the anechoic spaces in keeping with a venous malformation

compressible, and the typical history includes fluctuating size with activity, and gravity-dependent position. They can also be clinically suspected when the superficial component shows purple venous blebs (Fig. 4). The white pebbles of phleboliths are occasionally seen within a dilated vein in venous malformations, or felt by the sonographer's fingers during scanning. Venous malformations are episodically tender, usually from internal clot formation and sometimes stretching and distension. Venous malformations can also become more symptomatic during puberty and pregnancy, and this is secondary to increased intralesional clotting. Treatment typically includes image-guided sclerotherapy or surgical resection [20].

On sonography, venous malformations often present as compressible, well-marginated masses with a spongiform appearance from the presence of ectatic venous spaces separated by echogenic septa [21] (Fig. 5). Sometimes they appear as a multicystic mass resembling a lymphatic malformation (see next section; Fig. 6) and infrequently they show anechoic, tubular structures that can be easily recognized as vascular

channels [21] (Fig. 7). They are generally heterogeneous and mostly hypoechoic when compared with the adjacent subcutaneous soft tissues, although occasionally they appear isoechoic or hyperechoic [21] (Fig. 8). The detection of intralesional calcifications representing phleboliths is very helpful in the diagnosis of venous malformations (Fig. 5) because these are rare in other pediatric soft-tissue masses. However this sign's practical utility is often overstated because phleboliths are not common in pediatric venous malformations. Trop et al. [21] recognized phleboliths in only 16% of cases in their series and Paltiel et al. [6] in only 9%.

Doppler interrogation shows low vascular density, although it not infrequently has difficulty demonstrating intralesional vascularity (Figs. 6 and 8). The detection of flow can be enhanced by applying compression or performing the Valsalva maneuver [12]. Spectral Doppler analysis typically shows venous flow, although Trop et al. [21] reported absence of flow in 16% of their cases, even when optimizing the scanning technique. This apparent lack of vascularity is attributed either to very slow flow that is not detectable with conventional equipment or to extensive thrombosis of the venous
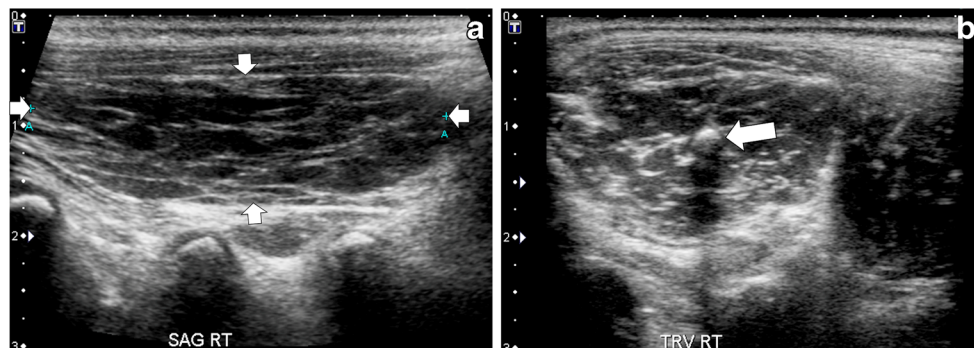
Fig. 5 Venous malformation in a 2-year-old girl who presented with a 6-month history of right paraspinal mass. **a** Longitudinal sonogram shows a well-defined intramuscular mass (*arrows*) that is heterogeneous from the presence of hypoechoic venous spaces separated by hyperechoic septa. This is the typical spongy appearance of venous malformations. **b** Transverse sonogram shows the presence of an intralesional calcification in keeping with a phlebolith (*arrow*)
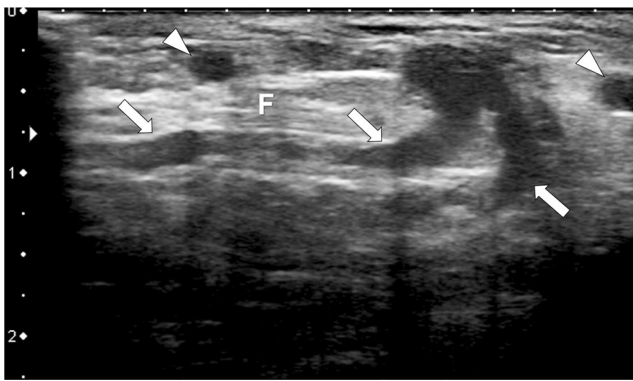
Fig. 7 Venous malformation in a 10-year-old girl who presented with intermittent swelling in the dorsum of the foot. Longitudinal sonogram shows anechoic, tortuous, tubular structures (*arrows*) and others with a more round shape (*arrowheads*), in keeping with large dysplastic veins as part of a venous malformation. Subcutaneous fat (*F*) is noted between the dysplastic veins

spaces. On occasion arterial flow can be detected, and this is thought to indicate the presence of a capillary malformation component (combined vascular malformation) [12, 21], but it could also just represent normal arteries coursing through the lesion or rarely a sign of intravascular papillary endothelial hyperplasia, also known as Masson tumor, which appears to be an abnormal response to thrombosis [22, 23].

Some venous malformations are intra-articular or juxta-articular with involvement of a joint, particularly the knee (Fig. 9). These used to be incorrectly referred to as synovial hemangiomas. The importance of making the diagnosis of these lesions is that they can cause repeated episodes of hemarthrosis, leading to synovial hypertrophy and damage of the articular cartilage and resulting in early development of osteoarthritis [24]. This involvement must be identified for treatment planning so that inadvertent passage of sclerosing agent into the joint during sclerotherapy does not occur
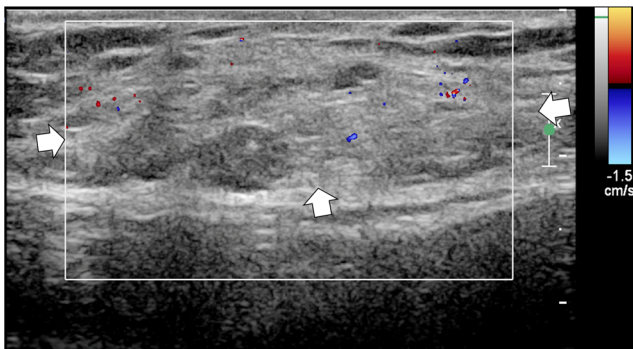
Fig. 8 Venous malformation in a 16-year-old girl who presented with a mass in the right upper arm. Color Doppler sonogram shows an irregular mass in the subcutaneous tissues (*arrows*) that is predominantly hyperechoic but contains a few hypoechoic areas. There is no significant vascularity in the lesion. This is an atypical presentation of venous malformation that could be confused with a microcystic lymphatic malformation or with a fat-containing mass. The final diagnosis was made with MR imaging

because this can result in joint damage. Surgical excision of these lesions is usually recommended.

There is therefore a wide spectrum of sonographic appearances of venous malformations which, along with atypical clinical presentations, can sometimes result in a diagnostic challenge. Further evaluation with MR imaging might be indicated in these situations.

Lymphatic malformation

Lymphatic malformations are subclassified into macrocystic, microcystic and mixed types. Some authors have proposed a size criterion to differentiate macrocystic from microcystic lesions, using as a cut-off value 1 cm or 2 cm, whereas other authors use as a criterion for macrocystic type the fact that the lesion can be successfully reduced in size with aspiration or sclerosis as opposed to the microcystic lesions, which cannot [25]. As with other disorders, the correct categorization of these lesions has a significant impact on which treatment options are offered. Lymphangioma is an old term used for lymphatic malformations that should be avoided because the suffix "-oma" should be reserved for proliferating tumors.

The typical clinical history of lymphatic malformation is of a lesion growing with the child, with episodic pain that is many times concurrent with viral illnesses or minor trauma. Some helpful clinical signs aid in the diagnosis of lymphatic malformation. The most helpful for microcystic lymphatic malformations is the presence of lymphatic vesicles, which can be found on the skin (Fig. 10) and on the mucosal surfaces of the oral cavity, where they are easily identifiable. Additionally, large exophytic, ecchymotic lesions are suggestive of macrocystic lymphatic malformations complicated with intralesional hemorrhage (Fig. 11). The treatment of microcystic lymphatic malformations has undergone a recent evolution with the introduction of mechanistic target of rapamycin (mTOR) inhibitors such as sirolimus, which have been found to be effective [26]. Image-guided bleomycin sclerotherapy and surgical resection can also be effectively used in select cases [27]. Surface lesions of the oral cavity and skin can be safely and effectively treated with carbon dioxide laser photoevaporation procedures, although the recurrence rate without concurrent medical therapy is high [20]. Image-guided sclerotherapy is usually the front-line treatment for macrocystic lymphatic malformations [28]. Mechanistic targets of rapamycin inhibitors are also used in certain clinical scenarios of widespread involvement, either primarily or as adjunctive therapy, whereas surgical resection is usually reserved as a second-line therapy.

Lymphatic malformations are more frequently found in the subcutaneous tissue, although involvement of multiple planes is not rare. Macrocystic lymphatic malformations appear as a lesion containing multiple cystic spaces that are separated
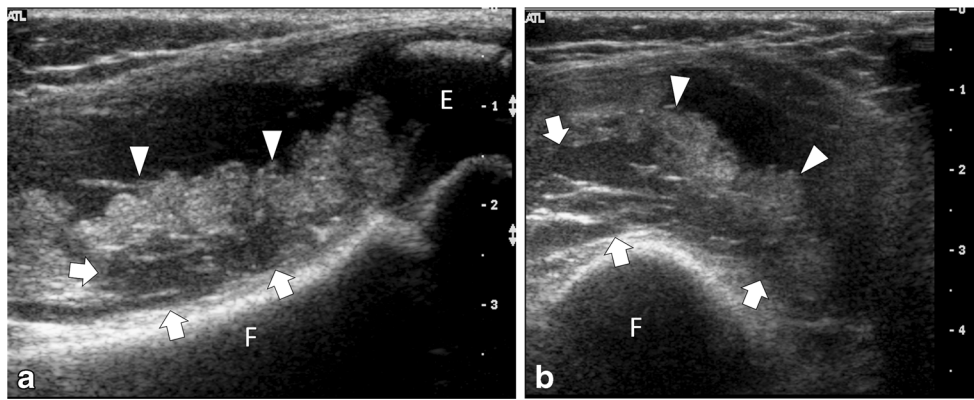
Fig. 9 Venous malformation in a 4-year-old girl who presented with repeated episodes of swelling of the right knee. **a** Longitudinal and (**b**) transverse sonograms of the right distal thigh and right knee show heterogeneous soft-tissue thickening in the suprapatellar recess. There are a hypoechoic component containing thin echogenic lines anterior to the distal femur (*F*) caused by venous malformation (*arrows*) and a more hyperechoic and lobulated component representing a combination of involvement of the synovium by venous malformation and secondary synovial hypertrophy (*arrowheads*). There is an associated knee joint effusion (*E*), likely representing hemarthrosis

from one another by thin septa. Compression with the transducer can deform the cystic spaces but they do not collapse, and this can be a helpful hint in the differentiation from venous malformations [29]. The cystic spaces can be anechoic (Fig. 12) or have varying degrees of echogenicity, sometimes with fluid-fluid levels, the latter more often seen when complicated with hemorrhage [7, 30] (Fig. 13). Fluid-fluid levels in vascular anomalies are not pathognomonic of lymphatic malformations because they can also be seen in venous malformations because of very slow flow with blood stagnation and formation of hematocrit levels [20]. Hematocrit levels represent stasis and layering of heavier cellular elements of blood dependent to liquid supernatant. Doppler interrogation of lymphatic malformations often reveals absence of flow or low vascular density with arterial or venous flow confined to the septa (Fig. 12). The flow should not be present within the cystic spaces, which would be more characteristic of a venous malformation. In case of superimposed infection, increased echogenicity and hyperemia of the adjacent soft tissues becomes evident and the fluid in the cystic spaces tends to be more echogenic.

Microcystic lymphatic malformations often appear as ill-defined hyperechoic lesions that contain scattered cystic spaces measuring less than 1–2 cm, although sometimes no cysts are visible (Fig. 14). The increased echogenicity is attributed to the multiple interfaces caused by tiny cysts that are beyond the resolution of the US equipment [7, 12]. Doppler interrogation shows absent flow or low vascular density.

Combined macrocystic and microcystic lymphatic malformations are not uncommon and show sonographic features of both types of lesions.
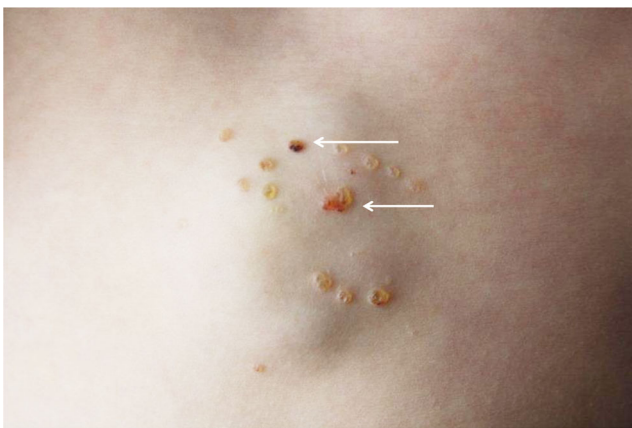
Fig. 10 Clinical photograph of microcystic lymphatic malformation in a 6-year-old girl who presented with painful swelling of the abdominal wall that had been intermittent for years and grew as she grew. Clinical exam shows numerous fluid-filled vesicles of the skin, some with internal hemorrhage and hematocrit levels (*arrows*), representing stasis and layering of heavier cellular elements of blood dependent to liquid supernatant. This is consistent with microcystic lymphatic malformation

Fig. 11 Clinical photograph of macrocystic lymphatic malformation in a 3-day-old girl who presented with rapidly growing chest wall masses and decreased hemoglobin requiring transfer to the neonatal intensive care unit. There is a right-side ecchymotic mass consistent with macrocystic lymphatic malformations, complicated by intralesional hemorrhage that required transfusion. The girl was successfully treated with image-guided doxycycline sclerotherapy
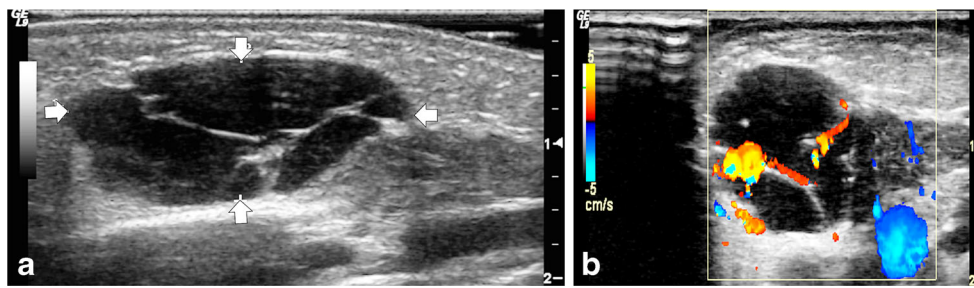
Fig. 12 Macrocystic lymphatic malformation in an 18-day-old boy who presented with a mass in the right shoulder. **a** Transverse sonogram shows a subcutaneous multicystic mass (*arrows*). The cystic spaces are anechoic and separated from one another by thin septa. **b** Longitudinal color Doppler sonogram shows flow that is confined to the septa, without flow in the cystic spaces

Sonographic mimickers of vascular malformations

We have described the main sonographic features that help in distinguishing the types of vascular malformations that are most frequently seen in children. However there are instances in which the differential diagnosis includes non-vascular tumors. Unfortunately the literature has mainly focused on this issue with regard to MR imaging, with very little information about sonographic appearances [23, 30].

As mentioned, venous malformations can sometimes have unusual nonspecific sonographic appearances, including the presence of intralesional arterial flow, making it difficult to exclude neoplastic lesions. Furthermore the clinical scenario might not be helpful, particularly in deep intramuscular lesions, which often present at a later age and are associated with pain — both red flags for neoplastic lesions [23]. In this situation, further investigation with MR imaging is the usual recommendation. In our experience sarcomas can mimic the gray-scale appearance of venous malformations because areas of necrosis and prominent vascular spaces can result in a hypoechoic spongy appearance, particularly with intramuscular lesions. However in this situation, Doppler sonography is usually extremely useful by showing a pattern of vascularity that is not typical for venous malformation, therefore alerting to the possibility of a neoplasm that requires further investigation with MR imaging.

Other neoplastic lesions can mimic the sonographic appearance of lymphatic malformations, particularly the macrocystic and combined types. These lesions include synovial sarcoma, epithelioid sarcoma and angiomatoid fibrous histiocytoma [30, 31]. To make the correct diagnosis, it is important to have a good clinical history and pay attention to the presence of thick septa and solid vascularized components, which raise suspicion for a neoplastic tumor because these are not usually seen in lymphatic malformations [30].

Complex and syndromic vascular anomalies

A long and heterogeneous list of entities is associated with vascular malformations, and many correspond to overgrowth syndromes. These are often better evaluated with MR imaging because of their commonly extensive involvement of the

Fig. 13 Macrocystic lymphatic malformation in a newborn boy with antenatal diagnosis of neck mass. Transverse sonogram of the right and anterior aspects of the neck shows a large complex mass composed of cystic spaces of different shapes and sizes, some anechoic and others hyperechoic from hemorrhage. A fluid-debris level is seen within a large cyst posteriorly (*arrows*). The fluid-debris level is vertically oriented because of the transducer position on the right side of the neck
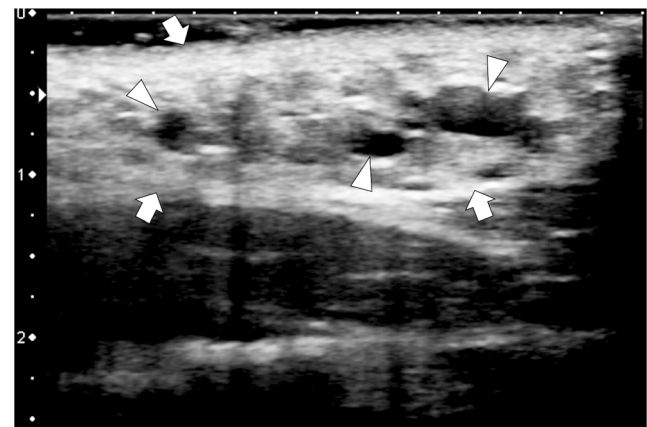
Fig. 14 Microcystic lymphatic malformation in a 10-year-old girl who presented with a 2-year history of slowly progressive swelling in the right axilla associated with cutaneous vesicles. Transverse sonogram shows an ill-defined subcutaneous lesion (*arrows*) that is predominantly hyperechoic and contains tiny cysts (*arrowheads*) measuring less than 1 cm

extremities, sometimes with extension into the trunk, and also because of their frequent association with other soft-tissue and bone anomalies including limb overgrowth [3, 32–34].

RASA1 gene mutation-related vascular anomalies

Mutations in the *RASA1* gene are found in entities that can present with high-flow vascular malformations. These include capillary malformation–arteriovenous malformation (CM-AVM) disorders, which are characterized by the presence of multiple cutaneous capillary malformations associated with underlying arteriovenous malformations [35]. Parkes–Weber syndrome is a specific type of CM-AVM that presents with limb overgrowth, more commonly affecting one of the lower extremities [33–35]. On clinical exam, the affected limb is very warm, showing a temperature discrepancy when compared with the unaffected limb. Typically pulsatility of the involved extremity is not appreciated. Common symptoms are exercise intolerance and arterial claudication from arteriovenous shunting and relative hypoxemia to the affected limb. Visually this manifests as non-healing ulcers of the involved extremity in advanced cases (Fig. 15).

Sonography can be helpful in assessing the increased flow to the affected extremity and in evaluating the more superficial arteriovenous malformations [35]. Sonography can also aid in diagnosis by showing arteriovenous malformations that lie deep to the clinically evident capillary malformations [36]. The arteriovenous shunting shows on Doppler interrogation with characteristic low-resistance arterial waveforms and pulsatile venous flow.

PTEN hamartoma tumor syndromes

Mutations in the *PTEN* tumor suppressor gene are now known to be the common underlying factor in both Bannayan–Riley–Ruvalcaba syndrome and Cowden syndrome and therefore these two conditions are now better referred to as *PTEN* hamartoma tumor syndromes [33]. These syndromes present with high-flow vascular anomalies that were traditionally regarded as arteriovenous malformations. However more recent observations have documented that these high-flow lesions correspond at histology with an overgrowth of an admixture of adipose tissue, fibrous tissue and abnormal blood vessels of various types [37, 38]. Kurek et al. [38] coined the term *PTEN* hamartoma of soft tissue (PHOST) for these lesions, although it is not clear whether they are true hamartomas or benign neoplasms. Associated clinical findings that help in the diagnosis include macrocephaly and developmental delay as well as a history of intestinal hamartomas. In boys, characteristic penile freckles might be seen. Recognition of a PHOST can be very important because it can be the first manifestation of *PTEN* hamartoma tumor syndromes, which are associated with


Fig. 15 Clinical photograph of Parkes–Weber syndrome in a 14-year-old girl initially diagnosed with Klippel–Trénaunay syndrome referred for an ultrasound exam after unsuccessful skin graft of the anterior thigh. Findings of capillary malformation, overgrowth and non-healing ulcers are noted (*arrows*), the latter consistent with Parkes–Weber syndrome, resulting in a change in the diagnosis and treatment. Endovascular embolization of arteriovenous fistulas was performed, with subsequent clinical improvement

a higher risk of developing certain malignant tumors, particularly of breast, thyroid, endometrium and kidney [38]. Treatment has traditionally been surgical for symptomatic lesions, although there are early reports of a possible role for mTOR inhibitors [39].

PHOST is usually multiple and the bulk of the lesion is in an intramuscular location although involvement of the adjacent fascial plane, subcutaneous tissue and dermis is common and occasionally might even cause disruption of underlying cortical bone [38]. There is typically disproportionate dilatation of the proximal veins draining the lesion. The sonographic appearance of PHOST has rarely been documented [15]. These lesions tend to be ill-defined, causing expansion and disruption of the affected muscle, and show heterogeneous echogenicity, being predominantly hyperechoic from the ectopic adipocytic tissue, and with visible large vessels on gray-scale images (Fig. 16). Color Doppler interrogation shows a high vascular density and spectral Doppler analysis shows features suggestive of arteriovenous malformation.

PIK3CA gene mutation-related syndromes

Somatic mosaic mutations of the *PIK3CA* (phosphatidylinositol-4, 5-biphospate 3-kinase catalytic subunit alpha) gene, now grouped as *PIK3CA*-related overgrowth
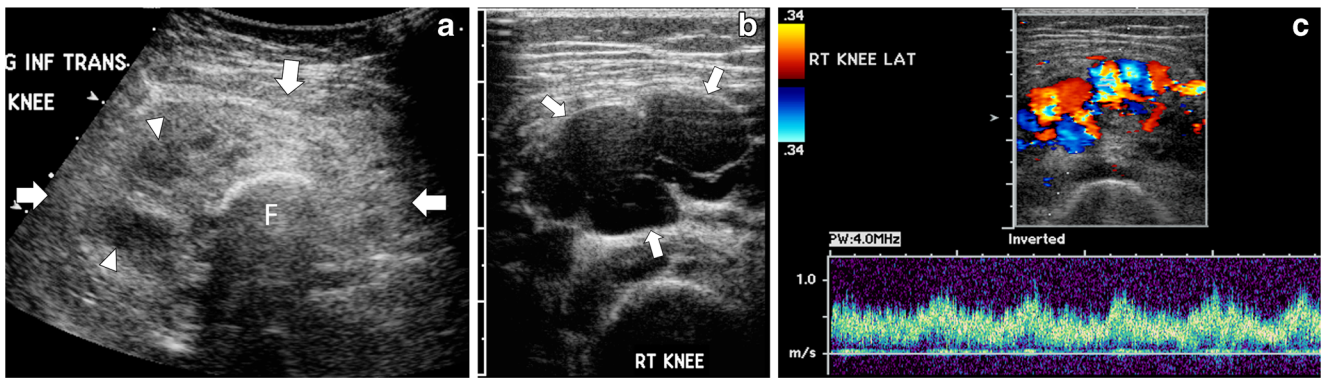
Fig. 16 *PTEN* hamartoma of soft tissue (PHOST) in a 7-year-old boy who presented with swelling of the right lower thigh and with a suprapatellar bruit on exam. **a** Transverse sonogram shows a large, ill-defined hyperechoic mass (*arrows*) within the quadriceps femoris muscle. The mass is heterogeneous and predominantly hyperechoic from fatty tissue, but it also contains hypoechoic areas representing large vessels (*arrowheads*). *F* femur. **b** Transverse sonogram shows a cluster of large vessels (*arrows*) within the mass, representing the typical large veins draining this type of lesion. **c** Transverse color Doppler sonogram and spectral Doppler analysis show multiple large vessels within the mass, some with pulsatile and turbulent venous flow from the anomalous arteriovenous communication. At the initial presentation, the diagnosis of atypical arteriovenous malformation was made. Subsequent genetic testing confirmed *PTEN* mutation, which is in conjunction with the imaging findings prompted the diagnosis of PHOST

spectrum, can manifest phenotypically as different entities presenting with vascular anomalies, including Klippel–Trénaunay syndrome, CLOVES (congenital lipomatous overgrowth, vascular malformations, epidermal nevi and skeletal anomalies) and fibro-adipose vascular anomaly (FAVA) [33]. Clinically these lesions can be suspected when marked overgrowth is identified and combined low-flow vascular anomalies are clinically evident [33, 40, 41]. When scanning these plaques of lymphatic vesicles and underlying phlebectasia with embryonic veins, one must be prepared for bleeding and have a hemostasis plan in the US division because these lesions can be quite friable and the authors have encountered this situation on multiple occasions.

Klippel–Trénaunay syndrome

Klippel–Trénaunay syndrome presents with capillary, venous and lymphatic malformations without high-flow lesions, commonly affecting one lower extremity, although bilateral cases, involvement of an upper extremity and extension into the trunk are not rare [32]. The classic triad includes capillary malformation, venous malformation/varicosities and limb overgrowth involving the bone and soft tissues (Fig. 17). The typical venous anomaly is the presence of a dilated vein in the lateral aspect of the thigh and lower leg, known as marginal vein of Servelle, seen in approximately 55% of the patients; this has been associated with a hypoplastic or interrupted lower limb deep venous system [32]. Sonography can be useful in evaluating localized venous or lymphatic malformations, demonstrating the venous anatomy and helping to evaluate patients with acute localized pain by showing thrombosis of the anomalous veins

(Fig. 18), an increasingly recognized cause of mortality and morbidity in this patient population [33].

CLOVES syndrome

CLOVES syndrome typically presents with a congenital truncal lipomatous mass that sometimes contains a lymphatic malformation (Fig. 19). In addition, venous malformations (phlebectasia) and less commonly arteriovenous malformations, frequently in paraspinal location, might also be present in addition to cutaneous and musculoskeletal anomalies such as epidermal nevus, hand and feet overgrowth, macrodactyly and sandal gap toe deformity [33, 40] (Figs. 19 and 20). There is no specific information regarding the role of sonography in CLOVES syndrome but it may be able to help in the evaluation of the aforementioned vascular anomalies.

Fig. 17 Clinical photograph of Klippel–Trénaunay syndrome in a 12-year-old girl who presented with bleeding from the lateral left thigh and history of pulmonary emboli. Note the soft-tissue overgrowth, associated plaques of lymphatic vesicles (*arrow*) and capillary malformation (*arrowheads*) along the entire leg, extending to the lateral foot. Embryonic veins were noted on sonography
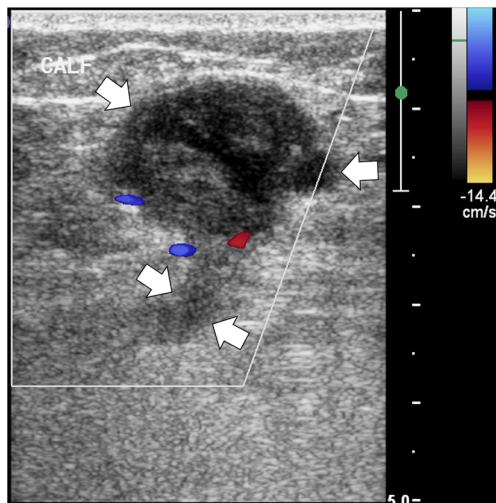
Fig. 18 Occlusive venous thrombosis in a 17-year-old boy with Klippel–Trénaunay syndrome who presented with acute pain localized to the right calf. Transverse color Doppler sonogram shows a large dysplastic vein occluded with thrombus (*arrows*)

Fibro-adipose vascular anomaly (FAVA)

FAVA is a complex mesenchymal malformation characterized by focal or diffuse intramuscular fibro-fatty replacement associated with low-flow vascular malformations — predominantly phlebectasia and less commonly lymphatic malformations — that can also affect the adjacent subcutaneous tissues but

usually without dermal involvement [42]. FAVA is more frequently seen as an isolated intramuscular lesion that can be very large, although occasionally it represents a complex combined vascular anomaly component of an overgrowth syndrome. The muscles most commonly affected are those in the calf, particularly the gastrocnemius, and in the forearm. Clinically these can present at any age with constant and severe pain.

Sonography shows an ill-defined hyperechoic intramuscular solid mass representing the fibro-fatty replacement [15, 42] (Fig. 21). Large veins are noted within the mass, which can extend into the overlying subcutaneous tissues and is sometimes complicated by thrombi.

AKT1 somatic gene mutation-related Proteus syndrome

Proteus syndrome is a rare condition characterized by progressive, segmental and disproportionate overgrowth that affects the dermis, fat, bones and central nervous system [41]. Mosaic somatic mutation of the *AKT1* gene has been found in more than 90% of patients with Proteus syndrome. These patients might have low-flow vascular malformations, including

Fig. 19 Clinical photograph shows typical findings in CLOVES syndrome, here in a 2-month-old boy with left upper extremity and chest wall lipomatous overgrowth. There is ecchymosis (*arrow*) from internal hemorrhage within a macrocystic lymphatic malformation. There is also a capillary malformation involving the right lower leg and foot as well as macrodactyly (*curved arrow*). *CLOVES* congenital lipomatous overgrowth, vascular malformations, epidermal nevi and skeletal anomalies

Fig. 20 Clinical photograph shows CLOVES syndrome in an 11-year-old girl with right lower limb asymmetrical overgrowth, capillary malformation on the lateral right thigh and sandal gap toe deformity in both feet. In addition, sonography showed an underlying macrocystic lymphatic malformation, which was causing pain and was successfully treated with image-guided doxycycline sclerotherapy. *CLOVES* congenital lipomatous overgrowth, vascular malformations, epidermal nevi and skeletal anomalies
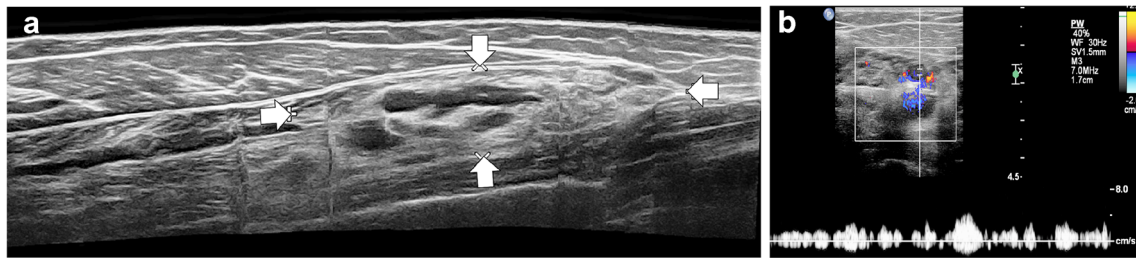
Fig. 21 Fibro-adipose vascular anomaly (FAVA) in a 14-year-old girl who presented with swelling and pain in the right calf. **a** Longitudinal sonogram using extended field-of-view technique shows a heterogeneous mass (*arrows*) within the gastrocnemius muscle. The mass is predominantly hyperechoic because of the presence of fibro-fatty tissue but also contains large vessels. **b** Transverse color Doppler sonogram and spectral Doppler analysis show that the vessels on gray-scale images are large veins, in keeping with the typical phlebectasia seen in FAVA. The sonographic findings were subsequently confirmed with MR imaging

capillary, venous, lymphatic and combined types. Some of the clinical manifestations overlap with those seen in CLOVES syndrome, although in Proteus syndrome there are no high-flow vascular malformations and the lipomatous mass is post-natal instead of congenital and can affect the extremities in addition to the trunk [40, 41]. Cerebriform nevus is the most characteristic skin lesion in children with Proteus syndrome [41] (Fig. 22).

There is limited information about the role of sonography in Proteus syndrome and because of its associated anomalies, MR imaging is the first-line modality in these children. However there are reports of sonography use in the detection of thrombi in enlarged peripheral veins in patients with Proteus syndrome [43].

findings and use of updated classification. However it is important to recognize that some entities, particularly venous malformations, can have a broad spectrum of appearances and that the diagnosis using sonography alone is sometimes limited. It is also noteworthy that sonography has a limited role in complex and syndromic vascular anomalies, mainly because of lesion extent, inherent characteristics of the lesion, and associated anomalies. MR imaging might be indicated in such cases.

Compliance with ethical standards

Conflicts of interest The authors have no financial interests, investigational or off-label uses to disclose.

Conclusion

Sonography is a useful tool in the evaluation of pediatric soft-tissue vascular malformations, providing valuable information for diagnosis and in some cases for monitoring treatment and complications. This requires close correlation with the clinical

Fig. 22 Proteus syndrome in an 8-year-old boy with classic cerebriform nevus (*arrow*) in addition to macrodactyly and spade-like widening of the left foot. On sonography there was marked isolated phlebectasia with slow flow in the same extremity

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