

Foam Sclerotherapy Treatment of a Venous Malformation of the Hand: A Further Confirmation of its Effectiveness

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Abstract

The term “vascular malformations” indicates a heterogeneous group of diseases of the circulatory system that can affect any type of vessel. “Venous malformations” represent a separate subgroup of vascular malformations originating from changes in the development of peripheral veins during the embryonic development. Generally, patients complain of a blue mass that grows over time and on examination, can be emptied by compression and/or arm elevation. Diagnosis is usually made by ultrasound and Magnetic Resonance Imaging, possibly augmented by further diagnostic tools in cases in doubtful cases. Management includes many options however; sclerotherapy is considered the gold standard for venous malformations. We report a patient who was treated successfully by means of direct foam sclerotherapy of the tumor with excellent results. We undertook a literature review of venous malformations to identify the optimal treatment, which confirmed that sclerotherapy is the best treatment option for these lesions.

Keywords: Venous malformations; Hand tumours; MRI; DUS; Foam sclerotherapy

Abbreviations: VMs: Venous Malformations; DUS: Duplex Ultrasound; MRI: Magnetic Resonance Imaging; MRA: Magnetic Resonance with Contrast Enhancement; ISSVA: International Society for the Study of Vascular Anomalies; ETFs: Extra-Truncular Forms; TFs: Truncular Forms; WBBPS: Whole Body Blood Pool Scintigraphy; Nd-YAG: Neodymium-doped Yttrium Aluminum Garnet; IPLS: Intense Pulsed Light Source; FLPD: Flash Lamp-Pumped Dye

Introduction

Vascular malformations represent a heterogeneous group of diseases of the circulatory system. Their protean nature is such that they may involve arteries, veins, lymphatics or capillaries, alone or in combination. They may affect any part of the body, often in association with other diseases or clinical syndromes. Vascular malformations are the fourth most common neoplasm in the upper extremity, accounting for 5% to 8% of hand tumors [1,2] only ganglions of the tendon sheath, mucous cysts and giant cell tumours occur more frequently. Today, the diagnostic approach is well established whereas the treatment has been evolving since the introduction of radiological and sclerotherapy occlusion in addition to the classical surgical and medical therapies.

Many studies provide support for foam sclerotherapy treatment and demonstrate its safety and effectiveness in treating such lesions.

This case report describes a young woman suffering from a superficial “low-flow” malformation of the left hypothenar eminence who was successfully treated by means of local foam sclerotherapy.

Case Report

A 28 year-old right-handed Caucasian woman, bartender, came to our outpatient’s clinic complaining of a swelling in her left hand,

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which had arisen some years before and had grown over time. She denied any trauma. The bulge had seldom been painful.

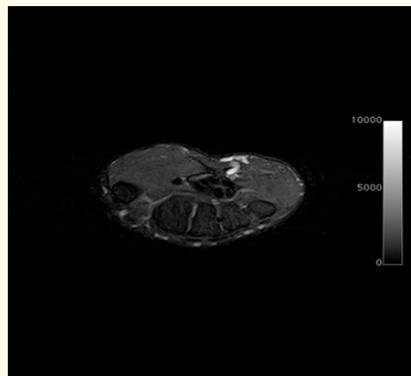
Her past medical history was unremarkable but she had shown a definite predisposition to developing keloid scarring as a complication of minor surgery. She had no smoking or alcohol abuse history.

On examination, she had a bluish mass in the subcutaneous tissue of the left hypothenar eminence (Picture 1). It measured 2 cm in diameter and was soft, not mobile and blanchable under pressure. Radial and ulnar pulses were normal, Allen test was negative and neurological examination was normal. After compression the patient experienced pain on the dorsal surface of the hand and wrist joint.



Picture 1: A Bluish Bulge on the Hypothenar Eminence is Evident.

She had a Magnetic Resonance Imaging (MRI) with contrast enhancement (MRA) that confirmed the presence of an ectatic (TD 3 mm) low-flow vascular structure in the subcutaneous tissue of the palmar surface of the hand at the carpo-metacarpal junction. It had a tortuous course, connecting small subcutaneous veins with some deeper venous branches close to the roof of the carpal tunnel, the communicating vascular bed was 8 mm wide and no definite communication channels with the radial artery were seen. On these findings, the lesion was considered most likely to be to a “venous angioma”.



Picture 2: FSE DP sequence on axial plan with fat saturation. On the superficial layer of the hypothenar eminence a VM with a collateral branch which, running deep close to the palmar aponeurosis connects with the ulnar side branches is evident.

Duplex Ultrasound (DUS) was not performed given the accuracy of MRA results.

After considering the clinical and MRA findings, and taking into account the risk of developing a disabling keloid scar on the palmar surface of her hand, she gave consent for foam sclerotherapy treatment.

Air (4 ml) and 1% Polidocanol (1 ml) were mixed using a three-way stopcock and the blend was injected through a 21G butterfly

needle (Picture 3). The patient experienced just a transient discomfort during the needle puncture but no other symptoms were observed during the injection. The area was packed with plain gauze and a compression dressing. The patient was allowed home after one hour and encouraged to resume her normal activities the following day.



Picture 3: Foam Injection into the Lesion.

On day 1 she was checked and the dressing removed. She had no symptoms whatsoever but for the mild pain observed preoperatively.

On day 9 (Picture 4), the patient returned to the clinic and her pain had reduced. No other symptoms were present. The mass had a grayish discoloration and was much less evident. She was advised to take painkillers.



Picture 4: The Lesion has almost disappeared.

On day 14 (Picture 5), the lesion appeared flattened and discolored. Mild pain was still present, though reduced, and the patient referred only occasional use of painkillers.

After one month the lesion had completely disappeared leaving the overlying skin only slightly darker than the surrounding area (Picture 6). She did not complain any pain.

After 3 months the picture was unchanged.



Picture 5: The Bulge Shows Regression.

Discussion

Vascular malformations are complex lesions with unpredictable behavioral characteristics. They can affect any vessel and sometimes represent a therapeutic challenge given their complexity in terms of variety, size and location. Vascular malformations are often serious and cause the patient severe disabilities given that they almost always appear during childhood and are difficult to eradicate despite the many treatment options available.

Epidemiology

The global incidence of vascular tumors is not known exactly but it is generally estimated between 4% and 10%. In 1993, Tasnadi reported an incidence of 1.2% in a study on 3573 three year-old children [3].

Etiopathogenesis

Vascular malformations etiopathogenic mechanisms remain unknown. They originate from defects in vessel development in the embryo, based on multifactorial genetic factors. In most cases they are sporadic occurring in individuals with no previous family history. On the other hand, hereditary forms are sometimes observed, related to genetic alterations of angiogenic factors that control vessel development. Two examples are given by familial muco-cutaneous and glomuvenous forms, in which the endothelial receptor TIE2/TEK for angiopoietin gene, contained in chromosome 9 and anomalies of the glomulin gene, localized on the short arm of chromosome 1, are seen respectively [4].

There is no sex preponderance although Upton and co., reported that vascular malformations are more common in females than males with a 1.5:1.0 ratio [5].

Classification

The common term “angioma” had been used until 1982, when Mulliken and Glowacki [6] proposed a classification of venous malformations, approved by the International Society for the Study of Vascular Anomalies (ISSVA) that included two categories: haemangiomas and malformations. Since its establishment, the ISSVA classification is actively replacing old eponyms. The subcategories recognized on the basis of clinico-genetic discoveries have been named following the ISSVA categorization rather than by creating new eponyms. The classification has been reviewed and modified in 1996 and in 2014 [7].

Table 1 lists the general part of a detailed classification of the vascular malformations categories, based on vessel type, location, pre-defined designation (i.e., Klippel-Trenaunay or Park-Weber syndromes) depth, extension, age of onset, severity, spontaneous regression rate, association with other anomalies, etc.

Among vascular tumours, haemangioma is the most common. It usually appears in newborns, showing rapid growth due to cellular proliferation, followed by inevitable involution. Haemangiomas show high-velocity flow in multiple vascular channels. Vascular malfor-

mations are also present at birth but, in contrast, grow proportionally with the patient. They are subdivided depending on the affected vessel type. When malformations affect more than one vessel, the combined lesions are named accordingly [6].

2014 ISSVA CLASSIFICATION OF VASCULAR ANOMALIES
Vascular Tumours
Benign
Locally aggressive or borderline
Malignant
Simple Vascular Malformations
Capillary malformations
Lymphatic malformations
Venous malformations
Arteriovenous malformations
Arteriovenous fistula
Combined Vascular Malformations
Capillary-venous malformations
Capillary-lymphatic malformations
Lymphatic-venous malformations
Capillary-arteriovenous malformations
Capillary-lymphatic-arteriovenous
Other combinations
Major Vessels Vascular Malformations
Vascular Malformations Associated With Other Anomalies

Table 1

Rheologically, they can be divided into “slow-flow” and “fast-flow” lesions, depending on their internal blood velocity and the type of vessel involved. The differentiation can be made by means of DUS and MRI or MRA.

Table 2 lists the six main types of venous malformations (VMs), of which our case is an example.

2014 ISSVA Classification Of Venous Malformations
Common venous malformation
Familial venous cutaneo-mucosal malformation
Bean syndrome (blue rubber bleb nevus)
Glomuvenous malformation
Cerebral cavernous malformation
Others

Table 2

VMs are usually low-flow lesions as they originate from changes in the development of veins, mainly low-flow vessels in the periphery. Conversely, fast-flow malformations are typically arterial or artero-venous.

Our case is best classified as a “low-flow common venous malformation” given the absence of family history and specific features typical of other vascular malformations categories, in addition to the clinical and MRI findings. VMs are the most frequent slow-flow vascular defects. They have been divided into three main categories by ISSVA: simple, combined and syndromic [8].

Venous Anomalies	Genetic	#, Localisation, Colour, Palpation	Other Features	Histology	Management
Simple					
Unifocal sporadic	Somatic activation TIE2 ¹ (49%)	solitary, all tissues and internal organs, normal to bluish colour, compressible, phleboliths	pain at awakening & effort, elevated D-dimer, local thrombosis, no PE	enlarged venous channels, flattened layer of endothelial cells, sparse smooth muscle cells	elastic compression, NSAID ⁴ , LMWH ⁵ , LD-ASA ⁶ , sclerotherapy, surgery
Multifocal sporadic	somatic activation TIE2 ¹	multifocal, mucosal, cutaneous and muscular, normal to bluish colour, less compressible			
VMCM	germinal activation TIE2 ¹	multifocal, mucosal & cutaneous, bluish colour, less compressible			
Combined					
Capillarovenous	unknown	solitary, cutaneous, subcutaneous, red to bluish-purple colour, capillary malformation overlying venous malformation, less compressible	pain at awakening & effort, elevated D-dimer	increased number of dilated capillaries + dilated venous-like channels with relative lack of smooth cells	laser, elastic compression, NSAID ⁴ , LMWH ⁵ , LD-ASA ⁶ , sclerotherapy, surgery
Capillary+Venous	unknown	capillary malformation & distant multifocal venous malformations, less compressible			
Lymphaticovenous	unknown	solitary, bluish-purple colour, lymphatic dermal vesicles & subcutaneous venous malformation, not compressible	lymphatic oozing & infection	lymphatic dermal vesicles + dilated venous-like channels with relative lack of smooth muscle cells	
Syndromic					
Klippel-Trenaunay	unknown	capillaro-lymphaticovenous malformation + limb hypertrophy	pain, elevated D-dimer level, PE ³	enlarged venous channels, flattened layer of endothelial cells, sparse smooth muscle cells	elastic compression, NSAID ⁴ , LMWH ⁵ , sclerotherapy, surgery
Blue Rubber Bleb Naevus	unknown	multifocal venous malformations, mucosal & cutaneous, hyperkeratotic bluish blebs on palms & soles	pain, elevated D-dimer, chronic anaemia, GI bleeding		

Maffucci	Unknown/ no PTHR1 ² mutation	multifocal, bluish nodules deforming hands & feet + multiple enchondromas	pain, normal D-dimer level, severe deformities of hands & feet, spont. fractures, malignancies	spindle cell haemangio-endothelioma + enchondroma	surgery
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- 1) TIE2: endothelial cell tyrosine kinase
- 2) PTHR1: Protein patched homolog 1
- 3) PE: pulmonary embolism
- 4) NSAID: non-steroid anti-inflammatory drugs
- 5) LMWH: low molecular weight heparin
- 6) LD-ASA: low dose aspirin

Table 3: Venous Anomalies: Clinical, Genetic and Histological Characteristics and Management.

Another system for categorizing VMs is the Hamburg classification (1988) [9,10]. VMs are divided into two groups, different for embryogenetic, anatomo-functional and clinical features: malformations involving dysplastic veins localized in the tissues distant from main veins, named “extra-troncular forms” and main veins malformations, named “troncular forms”.

Features	Extra-Troncular Forms	Troncular Forms
Frequency/Incidence	High	Low
Embryo genetic stage of appearance	Early	Late
Veins involved	Peripheral	Main
Proliferative degree	High	Low
Evolution	Progressive	Slow
Recurrence rate	High	Low
Haemodynamic effects	Low	High
Compression/infiltration	Common	Rare
Obstruction/reflux	Occasional	Common

Table 4: VMs Features according to Hamburg Classification.

Extra-Troncular Forms (ETFs)

ETFs represent the most frequent variety of VMs. They consist of dysplastic veins deriving from an error in the early phases of the embryonic vascular bed development and can be confined or extensively infiltrating. ETFs are composed of undifferentiated vessels of mesenchymal origin with a high degree of proliferation. Their evolution is progressive and they have an elevated recurrence rate after treatment. Furthermore, ETFs often cause compression or infiltration of the surrounding tissues.

Troncular Forms (TFs)

TFs are less common. They emerge in a later phase of embryogenesis and consist of anatomo-functional changes of variable severity involving the main vein trunks. TFs have a low proliferative degree with a limited recurrence rate after treatment but induce major haemodynamic effects on the district circulation, resulting in venous stasis due to obstruction and/or reflux. TFs are patchy malformations: this group also includes disorders such as valvular anomalies (absence or dysplasia), obstructions (atresia, aplasia, hypoplasia, intraluminal septa), dilations (venous aneurysms) and persistence of avascular embryonic veins (marginal vein, sciatic vein vein) [11-13].

Histopathology

The main cause of VMs is a disorder of the endothelium. The different types, unifocal, multifocal sporadic or familial, are characterized by enlarged venous channels lined by a single flattened layer of endothelial cells surrounded by sparse, irregularly distributed smooth muscle cells [14].

Dysplastic vessels show the typical features of veins and can vary according to the anatomical site. In soft tissues and skin, they are often wide with a definite muscular layer lacking the internal elastic lamina despite their richness in elastic fibers. The endothelium is flat and immuno-reactive to endothelial markers such as CD31 and CD34 but negative to WT-1 and GLUT-1 [15-17].

Some vessels show dilation with thinning of the wall and hematic intraluminal thrombus development which, over time, tend to form phleboliths. Some VMs are accompanied by a perivascular proliferation of cells normally found in vascular glomera, similar to smooth muscle cells and they are diagnosed as glomuvenous malformations [18].

Some VMs are familial, Vikkula and co., studied a mutation resulting in an arginine-to-tryptophan substitution at position 849 in the kinase domain of the receptor tyrosine kinase TIE2 segregates with dominantly inherited VMs in two unrelated families. Using proteins expressed in insect cells, they demonstrated that the mutation results in an increased activity of TIE2 and concluded that an activating mutation in TIE2 causes inherited VMs in the two families and that the TIE2 signaling pathway is critical for endothelial cell-smooth muscle cell communication in venous morphogenesis [19].

Clinical Considerations

The patient's clinical presentation and medical history are often enough to diagnose VMs. A mass emerged in childhood and grown over the years is likely to be a VM, mainly if it is a light-to-dark-blue lesion that can be emptied by compression and/or in the upright position. On clinical examination, thrills or bruits are not to be appreciated and on palpation, the affected area does not show any temperature change. VMs can affect any tissue or organ, such as skin, subcutaneous tissue, muscles, joints or intestine. VMs can be painful depending on size and location, physical exertion made and hormonal status of the patient or when thrombosis occurs [20].

Diagnosis

Diagnosis is based on DUS and MRI. DUS is useful to confirm slow-flow and to display vessels anatomy. VMs appear as hypoechoic or heterogeneous and compressible lesions in 80% of the cases [21].

MRI is the gold standard in planning the treatment of VMs. T1 and T2-weighted images portray the anatomic relation between the vascular lesion and adjacent organs, nerves, tendons and muscles. On T2-weighted sequences with fat saturation, VMs show hyper intense channels containing septations [22-24].

Further investigations, such as Magnetic Resonance Angiography (MRA), phlebography, plain X-ray, CT-scan or Whole Body Blood Pool scintigraphy (WBBPS) may be useful in particular cases (bone, multifocal, associated disseminated VMs, etc.) or when US and MRI are not enough to unravel diagnostic doubts.

Recently, Domp Martin and co., have demonstrated that VMs are the only disorders in which D-dimer is significantly high in the absence of other diseases. In healthy patients affected by vascular anomalies, an elevated D-dimer level is extremely suggestive of a VM: the Authors reported an incidence as high as 96.5%. Hence, D-dimer elevation can be considered as a useful biomarker for the differential diagnosis of vascular malformations [25].

Differential Diagnosis

Blue lesions on the skin are commonly classified as "angiomas". However, it is mandatory to identify the type of vascular malformation and exclude non-vascular lesions. Clinical features, such as patient's medical history, examination and DUS data should be enough to eas-

ily make the diagnosis. In doubtful cases MRI, either plain or with contrast enhancement and eventually histopathological examination is crucial.

Among blue lesions, dermal melanocytic nevus, subcutaneous haemangioma and hemorrhage within a lymphatic cyst or malformation can mimic a VM. Location, age of onset, tendency to disappear over the years, flow type and eventually histopathological examination are usually diagnostic.

Treatment

The therapeutic options in the management of VMs include medical treatment, surgical excision, laser, embolization and sclerotherapy, most of which are effective and safe [26]. The choice largely depends on the size and location of the mass and its association with other lesions.

Extensive VMs of the limbs should be treated initially with compression garments or stockings to reduce pain and the risk of thrombosis.

Medical therapy, including low-dose aspirin, anti-inflammatory drugs and Low-Molecular-Weight-Heparin (LMWH) appears to be effective, LMWH seems to be quite successful in reducing pain in patients with elevated D-dimer levels [27].

If conservative therapies fail, it is reasonable to try more aggressive treatments.

Surgical excision was the only non-medical option in the past but it yielded variable results in terms of limb function or cosmesis. Currently, its use should be limited to small peripheral VMs given the risk of morbidity or recurrences when treating bigger or combined lesions, particularly in vulnerable areas such as the hand and in close proximity to major nerves and arteries. Plain excision, purse-string suture, skin or fascio-cutaneous grafting and skin expanders have all been proposed [28].

Lasers were employed in medicine since the mid-1960s but the first reports on their use in the treatment of vascular malformations appeared in the early 1970s and were limited to superficial flat angiomas [29]. With improvements in laser technology, the extent and depth of skin lesions that could be treated with such a method increased. Argon and CO₂ devices, used at that time, were replaced by Neodymium-doped Yttrium Aluminum Garnet (Nd:YAG) lasers in the mid-1980s [30]. Later on, further techniques, such as intense pulsed light source (IPLS) [30], flash lamp-pumped dye (FLPD) [32] or diode [33] lasers, by means of extra or intra-lesional application, became available providing satisfactory results in deeper and larger VMs [34].

Chemical obliteration of VMs has been extensively performed. In the past, ethanol was the most used agent but it showed a high rate of complications due both to its intrinsic toxicity and the elevated doses needed for a satisfactory result [35]. Thus, many other sclerosing solutions have been studied, such as "absolute ethanol-zein-oleum papavaris" [36] or "ethylcellulose-ethanol" [37] combinations with good results.

Percutaneous sclerotherapy is considered to be the gold standard treatment of small (≤ 20 mm) subcutaneous VMs, as demonstrated by several Authors [38-43].

Many sclerosing agents and methods have been reported in the literature but Polidocanol, mixed at various concentrations with air or carbon dioxide [44-46] according to Tessari's technique [47], appears to be the most effective and safe [48]. 2% of patients, however, suffer from stroke, headache, scotoma and other neurological complications, confirming the potential risk of gas embolism intrinsic to the therapy [49,50]. Nevertheless, in small peripheral lesions the concentration and amount of drug injected are so small that the rate of complications is greatly reduced [51].

Conclusion

Foam sclerotherapy is an excellent therapeutic option in small VMs: high success and low complication rates have confirmed its effectiveness and safety and it is the procedure of choice for small lesions according to the literature.

This case adds further support to these data: the mass disappeared, the only symptom the patient experienced was a slight pain on the dorsal surface of her hand and wrist and she went back to her normal life the day after the procedure. Her symptoms resolved spontaneously within a few weeks and she required painkillers only occasionally. These problems were minor compared to the significant risk of hemorrhage and nerve damage associated with surgery. Eventually, our patient's tendency to form postoperative keloids and the associated risk of poor cosmetic and functional results, guided our choice to the safest therapeutic modality.

One to three injections are usually enough to completely treat VMs and the procedure can be performed in the outpatient clinic at low cost and reduced discomfort for the patient. In small VMs a single injection usually provides an excellent outcome.

In conclusion, data obtained from the literature and from our case confirm sclerotherapy as an excellent option for the treatment of VMs. However, further studies are required to assess indications, short and long-term results and complications.

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Conflict of Interest

No financial interest or any conflict of interest exists.

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