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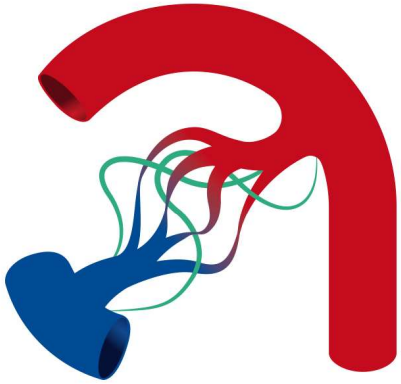
for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)



Venous malformation

Final Approved Patient Pathway by the Vascular Anomalies (VASCA) Working Group – 29/04/2020

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Disclaimer

- This document is an opinion statement reflecting strategies put forward by experts and patient representatives involved in the Vascular Anomalies (VASCA) Rare Disease Working Group of VASCERN.
- It is preferable that patients be evaluated in a multidisciplinary center specialized in the diagnosis and management of vascular anomalies.
- This pathway is issued on 29/04/2020 and will be further validated and adjusted as needed.
- Responsibility for care of individual patients remains with the treating physician.

Dieses Dokument wurde am 05.12.2022 von Dr. Friedrich Kapp für das Zentrum für Gefäßfehlbildungen (Uniklinik Freiburg) für das FZSE Freiburg geprüft, es war keine Kommentierung notwendig. Eine gemeinsame Überprüfung und Diskussion wird unabhängig hiervon in VASCA-WG erfolgen.

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Suspected Venous Malformation

- Blue or skin coloured swelling; sometimes mucosal lesion
- Typically empties with compression and fills up in dependent position
- Painful at awakening or after exercise. For extended period if local thrombosis (1 to 2 weeks)
- Sometimes : firm, painful on palpation and/or palpable phleboliths
- No thrill, not warm
- Number of lesions, associated anomalies and/or limb hypo / hypertrophy
- Family history

- Doppler ultrasound to confirm diagnosis & exclude fast flow
- MRI if diagnosis unclear
- Biopsy rarely needed for differential diagnosis

- Sporadic Unifocal → A
- Sporadic Multifocal → B
- Familial Multifocal → C
- Combined and/or Syndromic → D

Histology :

- **VM : dilated veins, sparse vascular smooth muscle cells**
- **GVM : veins surrounded by glomus cells**
- **Maffucci syndrome : spindle cell hemangioma**
- **VVM: clusters of venus-like channels, GLUT 1+**

VM :Venous Malformations
GVM: Glomuvenous Malformations
VVM: Verrucous Venous Malformations

LEGEND: Clinical evaluation | Investigations | Treatment | Associated Genes

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Venous Malformation Diagnostic Work-Up continued

A **Sporadic Unifocal**
Majority of VMs
No family history

→ Somatic TEK or PIK3CA → **1** **Sporadic Unifocal Venous Malformation**

B **Sporadic Multifocal**
Less compressible
Number increases with time
No family history

→ Small bluish or skin coloured lesions, involving skin, mucosa or sometimes muscle
Somatic TEK → **2** **Sporadic Multifocal Venous Malformation**

→ One large VM at birth
Multiple small blue-to-purple "rubbery blebs" disseminated in entire body including GI tract, evolving over time
Sometimes subcutaneous, mucosal or hyperkeratotic lesions typically on palms and soles
Anaemia
Somatic TEK → **3** **Blue Rubber Bleb Nevus Syndrome (BRBN)** → Anaemia : GI endoscopy

→ Hard bluish nodules
Hand and foot deformities
No coagulation abnormality
Somatic IDH1 and 2 → **4** **Maffucci syndrome** → X Ray hands and feet : enchondroma

→ Single or multiple hyperkeratotic papules; can enlarge ; mainly on extremities (legs++)
Somatic MAP3K3 → **5** **Verrucous Venous Malformation (VVM)**

For all types of VMs
Evaluate : Pain, aesthetic and functional risk

For all types of VMs
Coagulation status (D Dimer, fibrinogen)
MRI :
- if treatment is considered
  - to anticipate complications
  - to characterize the VM: size and extent (e.g. muscles, joints, bones, organs)
  - if genital or perineal location MRI of the pelvis to rule out internal vascular malformation

Genetics :
somatic = mutation
only in affected tissue (need biopsy)

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Venous Malformation Diagnostic Work-Up continued

C **Familial Multifocal**
Small lesions
Less compressible
Number increases with time
Family history

Small bluish or skin coloured lesions, involving skin, mucosa or sometimes muscle
Germline TEK
→ 6 **Venous Malformation Cutaneous Mucosal (VMCM)**

Dark blue or purple plaques, nodules
Superficial skin lesions
Painful on palpation
No coagulation abnormality
Germline Glomulin
→ 7 **Glomuvenous Malformation (GVM)**

Dark blue or purple papules
Often hyperkeratotic, Not painful on palpation
Seizures, headaches, cerebral hemorrhages, focal neurological deficit.
Germline KRIT 1/CCM1
→ 8 **Hyperkeratotic Cutaneous Capillaro-Venous Malformation (HCCVM)**
→ Cerebral MRI : cavernoma

For all types of VMs
Evaluate : Pain, aesthetic and function

For all types of VMs
Coagulation status (D Dimer, fibrinogen)
MRI :
- if treatment is considered
  - to anticipate complications
  - to characterize the VM: size and extent (e.g. muscles, joints, bones, organs)
  - if genital or perineal location MRI of the pelvis to rule out internal vascular malformation

D **Combined and/or Syndromic**

Digital anomalies
Epidermal naevi
Hypertrophy / overgrowth or Hypotrophy
Lipomas
Macrocephaly
Neurological anomalies
Other Vascular malformations
→ 9 **Klippel-Trénaunay, CLOVES, Proteus, PHTS**
→ Refer to Overgrowth Pathway

Genetics: germline mutation : blood test

Management of VM : next page

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Venous Malformation Management/Treatment

1 Sporadic uni or multifocal VM Small skin and mucosal lesions

2 Sporadic Uni or multifocal VM Large skin and mucosal lesions

6 Familial multifocal VMCM

Common management approaches

Conservative treatments:
- Elastic compression (except GVM and Maffucci)
- Nd:YAG Laser for superficial lesions
- Treatment of consumptive coagulopathy (next page)
- Non-steroidal anti-inflammatory drugs (NSAID)

Invasive treatments :
- Surgical management
- Sclerotherapy (alone or in combination with surgery)
- Intralesional Diode or Radiofrequency intralesional
- Cryoablation

Emerging treatment option :
- Sirolimus

3 Sporadic multifocal BRBN → Anemia : iron supplementation, blood transfusion

7 Familial multifocal GVM → Prefer laser for "plaque-like lesions"

5 Verrucous Venous Malformation (VVM) → Prefer surgical resection or laser

8 Hyperkeratotic Cutaneous Capillaro-Venous Malformation (HCCVM) → Neurologic monitoring

4 Sporadic Multifocal « Spindle cell Hemangioma » : Maffucci syndrome → Prefer surgical resection Cancer monitoring

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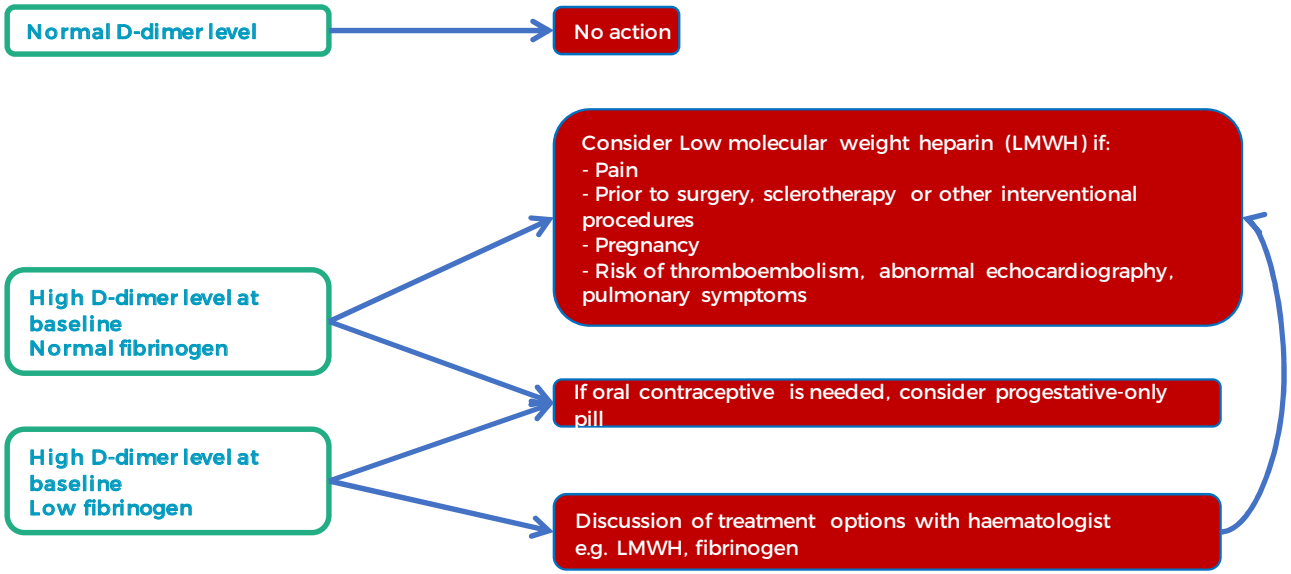
Chronic Consumptive Coagulopathy Management



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to patients with rare vascular diseases

VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases, is dedicated to gathering the best expertise in Europe in order to provide accessible cross-border healthcare to patients with rare vascular diseases (an estimated 1.3 million concerned). These include arterial diseases (affecting aorta to small arteries), arterio-venous anomalies, vascular malformations, and lymphatic diseases.

VASCERN currently consists of 30 highly specialised multidisciplinary Healthcare Providers (HCPs) from 11 EU Member States and of various European Patient Organisations and is coordinated in Paris, France.

Through our 5 Rare Disease Working Groups (RDWGs) as well as several thematic WGs and the ePAG– European Patient Advocacy Group, we aim to improve care, promote best practices and guidelines, reinforce research, empower patients, provide training for healthcare professionals and realise the full potential of European cooperation for specialised healthcare by exploiting the latest innovations in medical science and health technologies.

More information available at: https://vascern.eu

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