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.
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

LEGEND:
- Clinical evaluation
- Investigations
- Treatment
- Associated Genes

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
Venous Malformation Diagnostic Work-Up continued

**A: Sporadic Unifocal**
- Majority of VMs
- No family history
- Somatic TEK or PIK3CA

**B: Sporadic Multifocal**
- Less compressible
- Number increases with time
- No family history
- Somatic TEK

1. **Sporadic Unifocal Venous Malformation**
   - Small bluish or skin coloured lesions, involving skin, mucosa or sometimes muscle
   - 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

2. **Sporadic Multifocal Venous Malformation**
   - Hard bluish nodules
   - Hand and foot deformities
   - No coagulation abnormality
   - Somatic IDH1 and 2

3. **Blue Rubber Bleb Nevus Syndrome (BRBN)**
   - Spontaneous TEK
   - Single or multiple hyperkeratotic papules; can enlarge; mainly on extremities (legs+++)
   - Verrucous Venous Malformation (VVM)

4. **Maffucci syndrome**
   - X Ray hands and feet: enchondroma

5. **Verrucous Venous Malformation (VVM)**
   - Associated Genes

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

Anaemia: GI endoscopy

Clinical evaluation
Investigations
Treatment
Associated Genes

**LEGEND:**
- Clinical evaluation
- Investigations
- Treatment
- Associated Genes

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Venous Malformation Diagnostic Work-Up continued

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

**Germline TEK**
- Small bluish or skin coloured lesions, involving skin, mucosa or sometimes muscle

**Dark blue or purple plaques, nodules**
- Superficial skin lesions
- Painful on palpation
- No coagulation abnormality

**Germline Glomulin**
- Dark blue or purple papules
- Often hyperkeratotic, not painful on palpation
- Seizures, headaches, cerebral hemorrhages, focal neurological deficit

**Germline KRIT 1/CCMI**
- Digital anomalies
- Epidermal naevi
- Hypertrophy / overgrowth or Hypotrophy
- Lipomas
- Macrocephaly
- Neurological anomalies
- Other Vascular malformations

**Venous Malformation Cutaneous Mucosal (VMCM)**

**Glomuvenous Malformation (GVM)**

**Hyperkeratotic Cutaneous Capillary-Venous Malformation (HCCVM)**

**Klippel-Trénaunay, CLOVES, Proteus, PHTS**

**Cerebral MRI : cavernoma**

**Management of VM : next page**

**Legends:**
- Associated Genes
- Clinical evaluation
- Investigations
- Treatment
- Associated Genes

For all types of VMs
- Coagulation status (D Dimer, fibrinogen)
- MRI:
  - 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

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

Venous Malformation Diagnostic Work-Up continued
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
3. Sporadic multifocal BRBN
4. Sporadic Multifocal
   - Spindle cell Hemangioma »: Maffucci syndrome
5. Verrucous Venous Malformation (VVM)
6. Familial multifocal VMCM
7. Familial multifocal GVM
8. Hyperkeratotic Cutaneous Capillaro-Venous Malformation (HCCVM)

Common management approaches:

- Conservative treatments:
  - Elastic compression (except CVM 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)
  - Intraliesional Diode or Radiofrequency intraliesional
  - Cryoablation

- Emerging treatment option:
  - Sirolimus

Associated Genes:

LEGEND:

- Clinical evaluation
- Investigations
- Treatment
- Associated Genes

- Anemia: iron supplementation, blood transfusion
- Prefer laser for "plaque-like lesions"
- Prefer surgical resection or laser
- Neurologic monitoring
- Prefer surgical resection
- Cancer monitoring
Chronic Consumptive Coagulopathy Management

**LEGEND:**
- Normal D-dimer level
- High D-dimer level at baseline
- Normal fibrinogen
- High D-dimer level at baseline
- Low fibrinogen

**Clinical evaluation**

**Treatment**
- Consider Low molecular weight heparin (LMWH) if:
  - Pain
  - Prior to surgery, sclerotherapy or other interventional procedures
  - Pregnancy
  - Risk of thromboembolism, abnormal echocardiography, pulmonary symptoms

**Investigations**

- If oral contraceptive is needed, consider progestative-only pill

- Discussion of treatment options with hematologist e.g. LMWH, fibrinogen

No action
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.

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