Clinically Relevant Hematologic Concerns in Venous Malformations

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The hematology of venous malformations
- originally thought to be relatively benign hematologically
- first described Enjolras and Mazoyer
- they noted the association of a distinct coagulopathy within a subset of purely venous malformations that was distinct from Kasabach-Merritt phenomenon i.e. platelets were not consumed

VMs and Virchow’s Triad
- venous malformations provide a unique local environment that provokes the normal coagulation cascade
- structurally abnormal endothelium
- functionally abnormal endothelium
- repeated injury due to hemorrhage or clotting

Localized Intravascular Coagulopathy (LIC)
- normal PT
- normal aPTT
- normal platelet count
- some have low fibrinogen levels (<150 mg/dL or 1.5 g/L)
- many will have elevated D-dimer levels (> 0.5 μg/ml or 500 μg/L)
- elevated FDPs (> 10 μg/ml or 10 mg/ml)
**Prevalence of LIC in Venous Malformations**

- 88% of patients
- "decreased fibrinogen and soluble complexes"
- elevated fibrin split products
- moderately low platelet count


**86% of patients**
- decreased fibrinogen and soluble complexes
- elevated fibrin split products
- moderately low platelet count


**42% elevated D-dimers, 61% were over 1.0 mg/ml**
4.3% had low fibrinogen


**2017, 2018, 2019 patients**
- 33% elevated D-dimers
- 58% elevated D-dimers
- abnormal von Willebrand issues


2015, 70 patients, 37 with LIC

**MRI phenotypes of localized intravascular coagulopathy in venous malformations**

2017, 24 patients

2018, 18 patients

2019, 18 patients

**Relationship between LIC and VM characteristics**

**MRI phenotypes of localized intravascular coagulopathy in venous malformations**

2015, 70 patients, 37 with LIC

**Association of Localized Intravascular Coagulopathy With Venous Malformations**
Why is LIC clinically relevant?

- although commonly asymptomatic, flare ups can lead to
  - pain
  - thrombosis and focal swelling
  - bleeding
  - over time, palpable lumps and phlebolith formation can ensue
  - sustained can lead to more serious thromboembolic events
  - superficial thrombophlebitis
  - DVT, PE, pulmonary HTN


So, . . .

How and when do we intervene clinically to address hematologic issues?

Which parameters in which clinical setting are important?

How do we stratify risk of major hematologic deterioration or complications?

5 points . . .

1. Conservative treatment

encourage activity

avoidance of activities eliciting symptoms

graduated compression garments

- can provide symptomatic relief of pain, slow progression of the lesion size, and can lower risk of ulceration
- can decrease LIC/pain by decreasing blood pooling/volume of VMs
- must be consistently used and modified with patient growth


3. Diagnosis of non-overt disseminated intravascular coagulation made according to the International Society on Thrombosis and Haemostasis criteria with some modifications. Korean J Hematol 2010;45:260-263.

4. D-dimer levels > 0.5 μg/ml
  - FDPs > 10 μg/ml
Heparin and anti-Xa therapy

When to use LMWH?: Assess risk

Intervention: Sclerotherapy or Surgery

Chronic Therapy in VMs

DOACs


Low molecular weight heparin can be used both to treat the pain caused by LIC and prevent decompensation of severe LIC to DIC.

When to use LMWH?: Assess risk

- all VMs
  - large size
  - multi-focal
  - venous ectasia
  - overgrowth synd
  - combined lesions
  - assess risk

D-dimer
PT - aPTT
fibrinogen
CBC

KTS
LVM/BRBN
CLOVES

Conservative

PRE: give LMWH:
0.5 mg/kg SC BID x 1 week
check labs x 1 more week
POST: give LMWH:
LONGEST of:
same dose x 2 wk
until ambulating

Chronic Therapy in VMs

- all VMs
  - large size
  - multi-focal
  - venous ectasia
  - overgrowth synd
  - combined lesions
  - spongiform
  - truncal

Conservative

Early work in the use of DOACs in LIC shows promise.
Aspirin and Vit K for LIC

- there is some retrospective evidence that treating with aspirin may reduce pain by reducing platelet aggregation in the lesion
- not easily used in pediatric population
- not well correlated with laboratory investigations
- unknown if it reduces risk of more serious thrombotic complications
- anecdotal reports describe Vitamin K antagonists usage