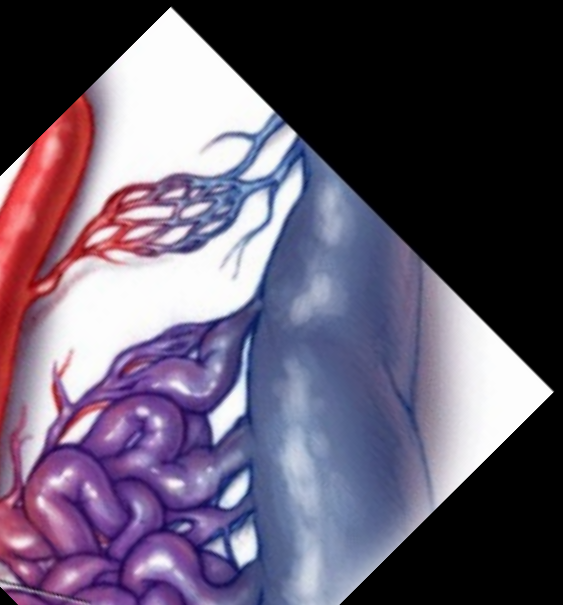
Addressing Thrombosis risk in patients with Vascular Malformations including CLOVES Syndrome.



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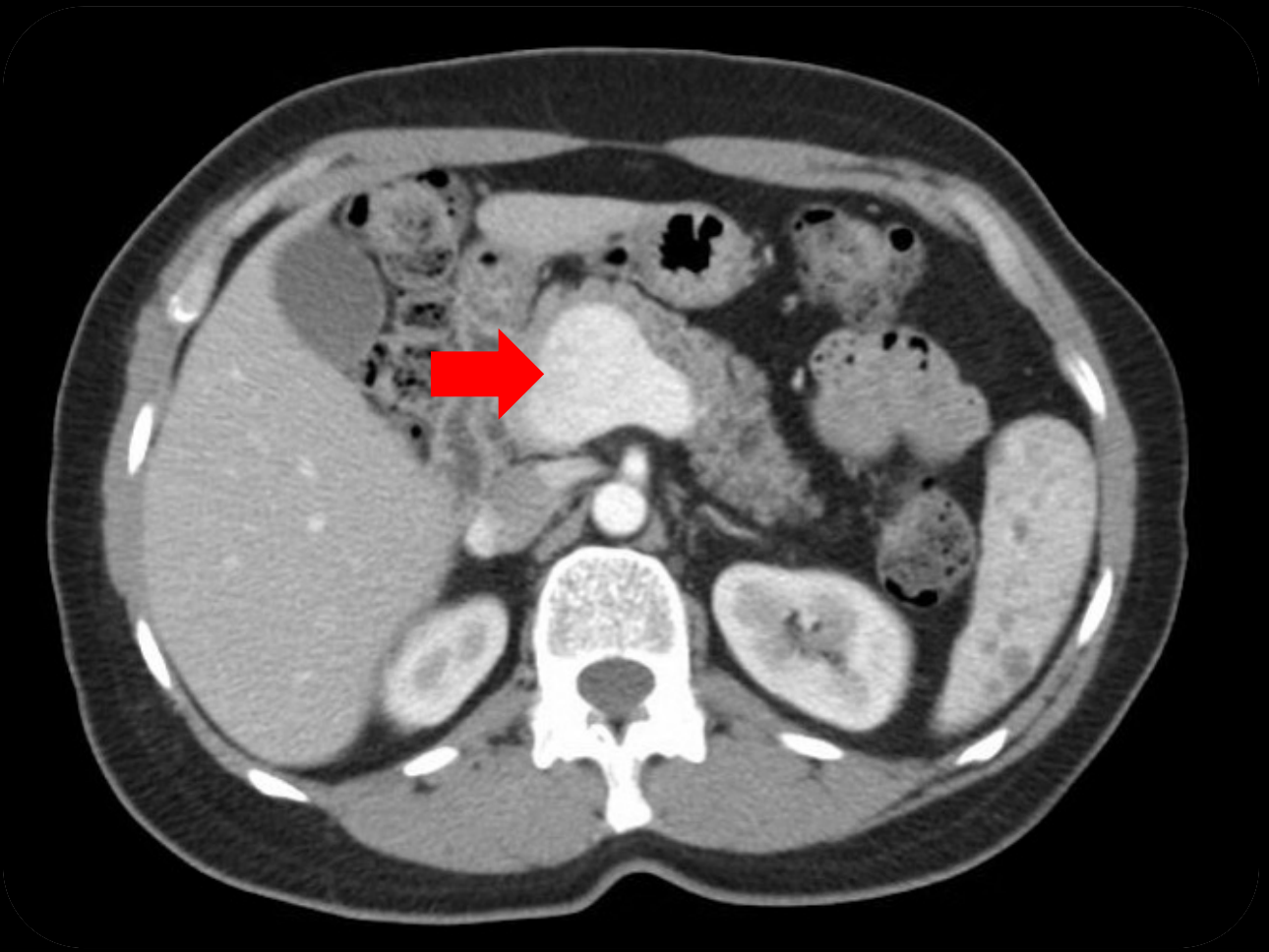
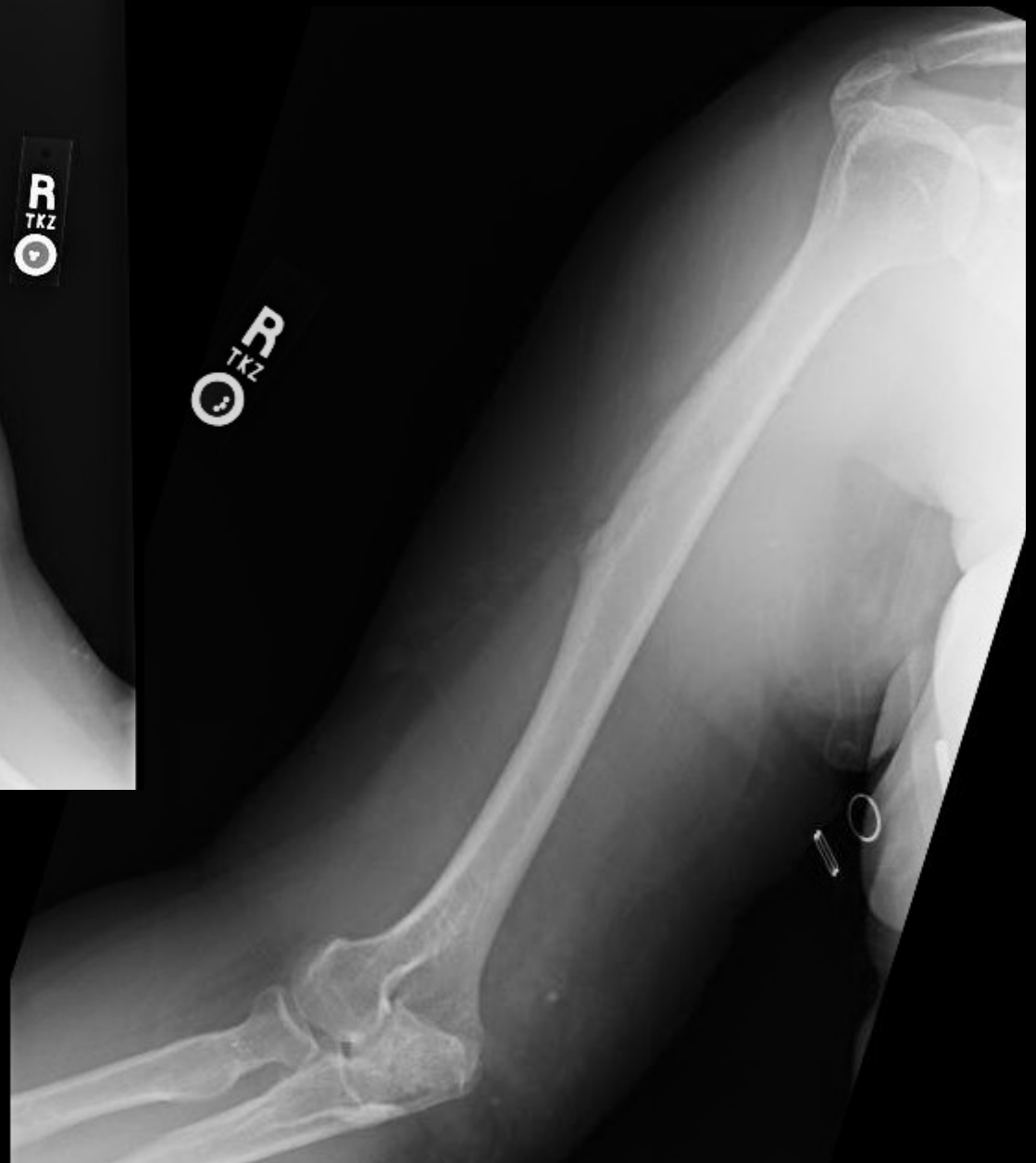


Patient referred,

Massive portal vein aneurysm.

R
TKZ


R
TKZ

L
MM

R
MM

Congenital

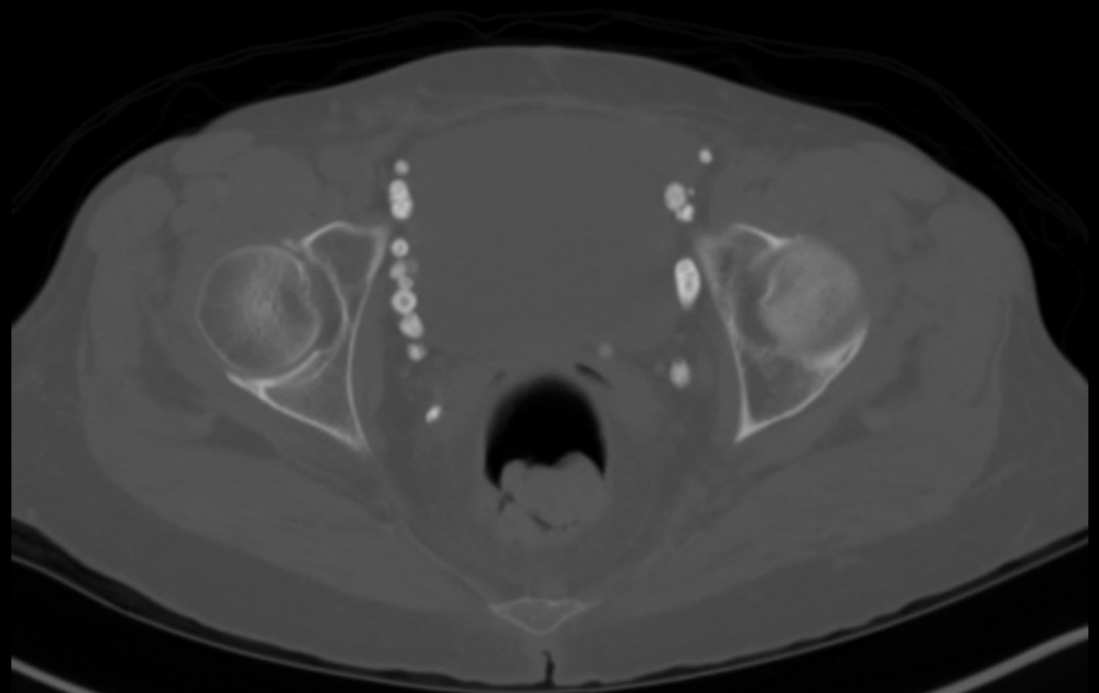
Lipomatous

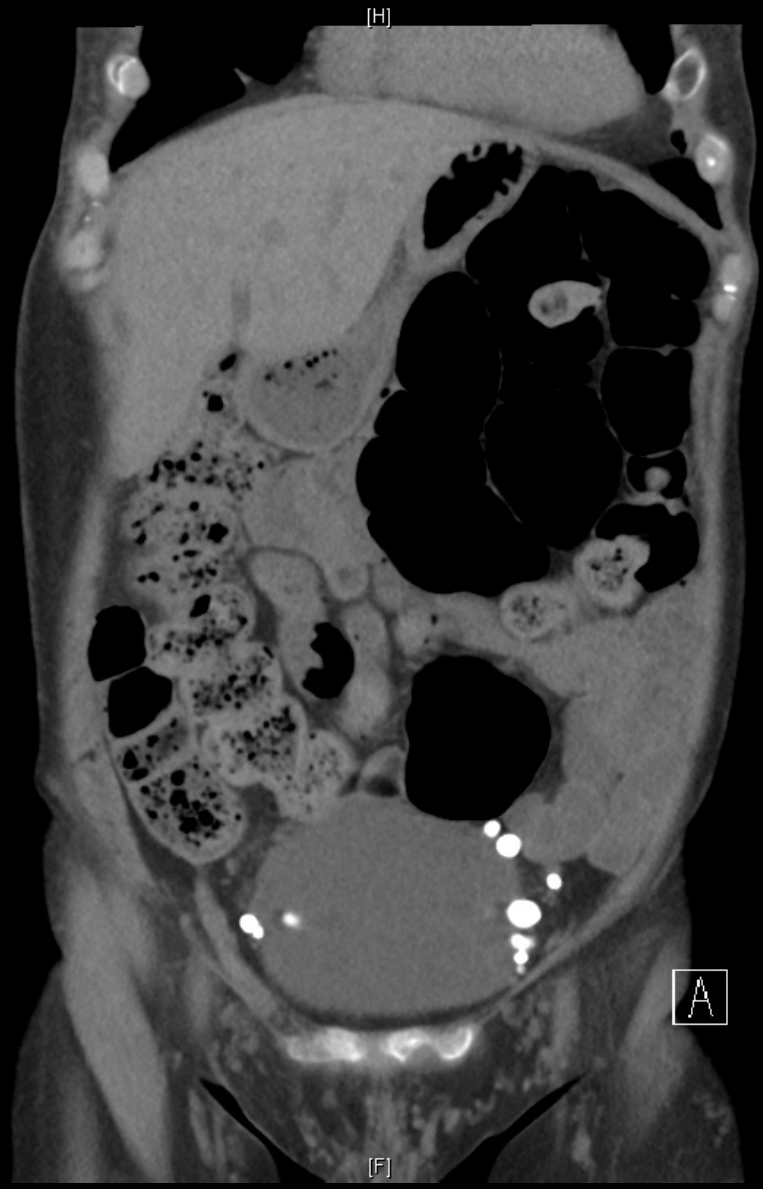
Overgrowth

Vascular Malformation

Epidemal Naevi

Spinal/Skeletal anomalies.





CLOVES Syndrome

The lipomatous lesions are often infiltrative and tend to recur following resection.

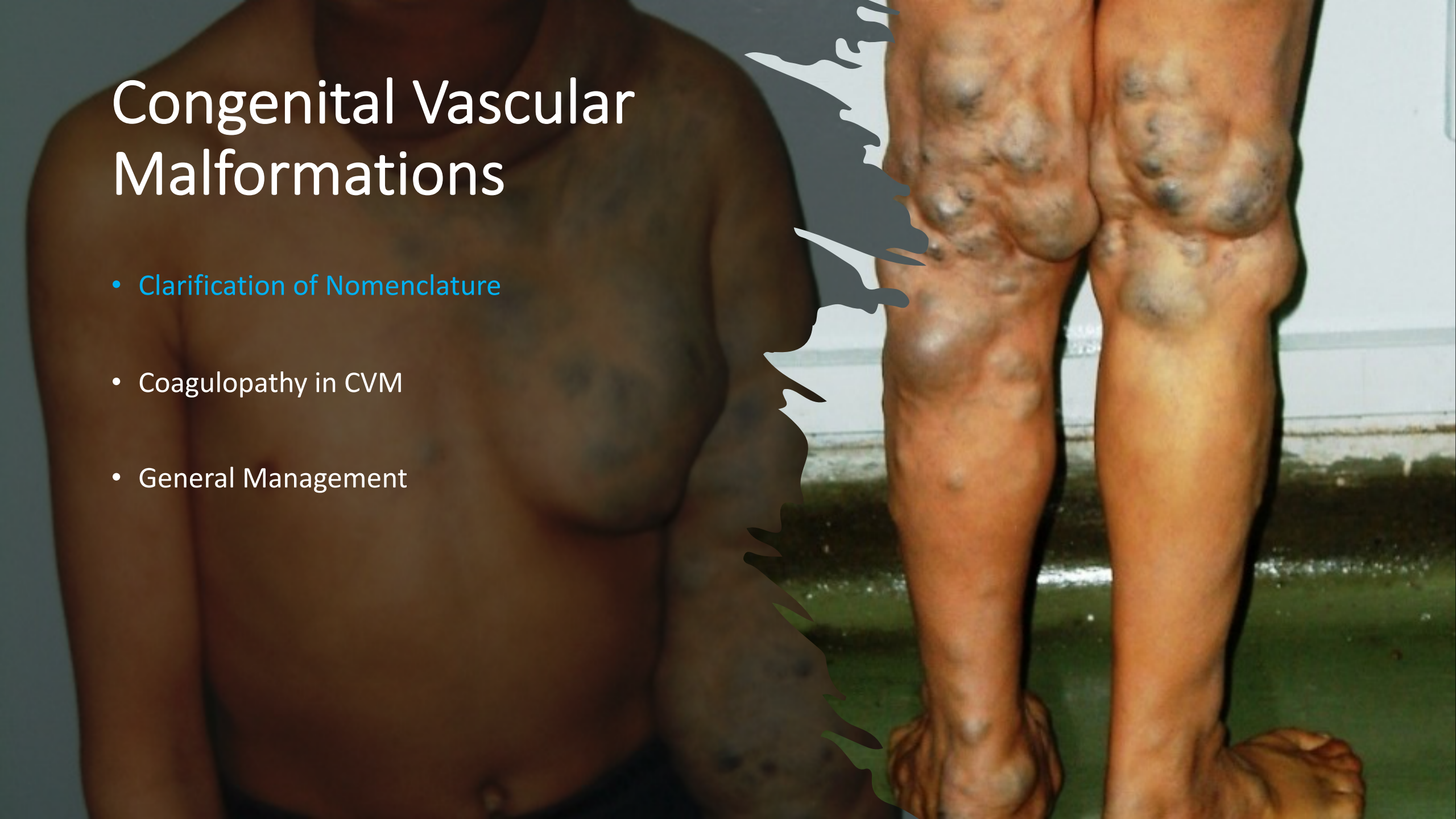
Skeletal overgrowth and malformation are common in the extremities, as is scoliosis.

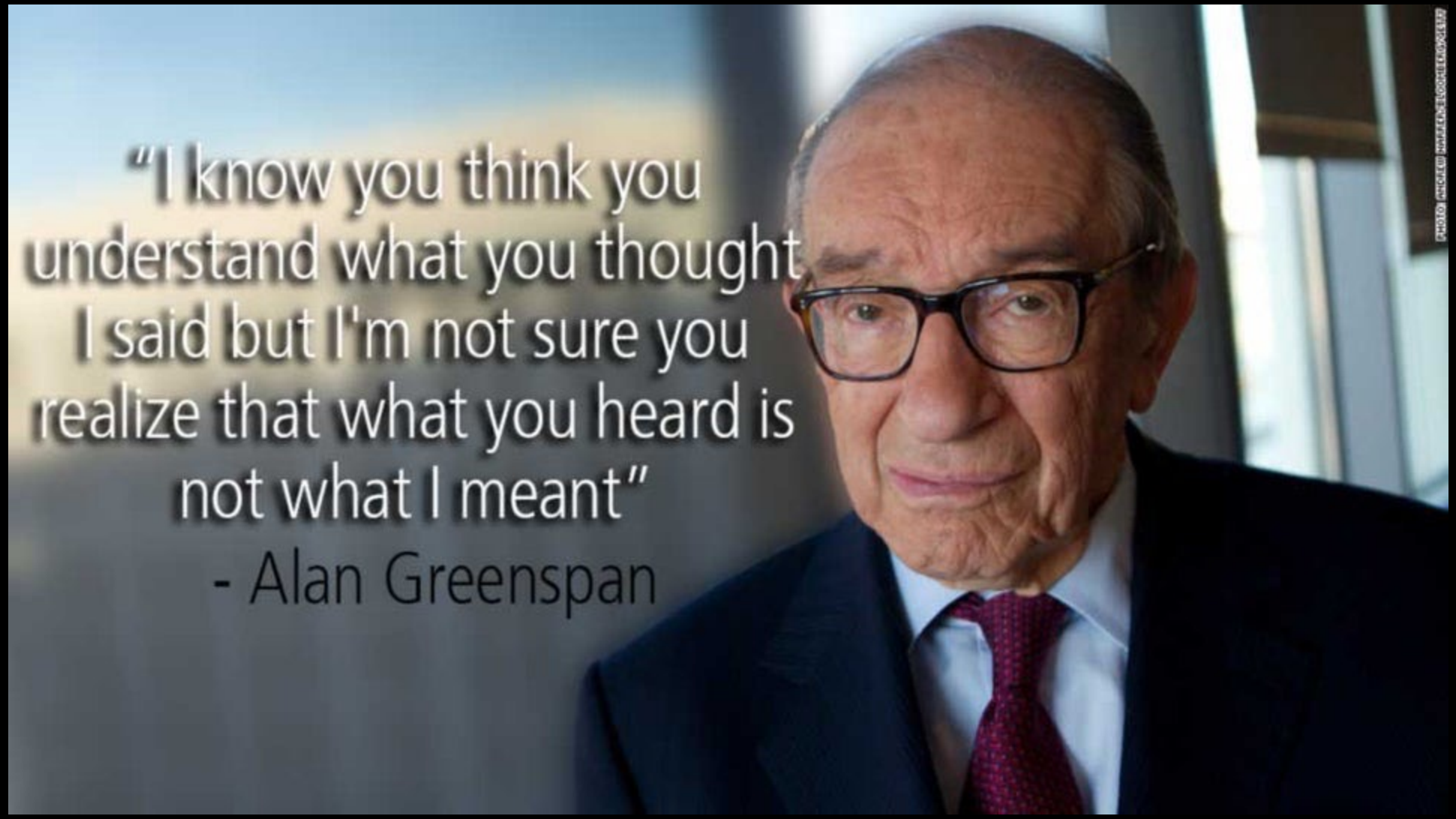
Vascular lesions include capillary, lymphatic, venous and arteriovenous malformations .

In contrast to the Proteus and BRRS syndrome there is no mental impairment

Congenital Vascular Malformations

- Clarification of Nomenclature
- Coagulopathy in CVM
- General Management




"I know you think you understand what you thought I said but I'm not sure you realize that what you heard is not what I meant"
- Alan Greenspan

- Venous malformation (VM) is one of the congenital vascular malformations (CVMs) with ‘limited’ involvement to the venous system only as the outcome of defective development during various stages of embryogenesis.

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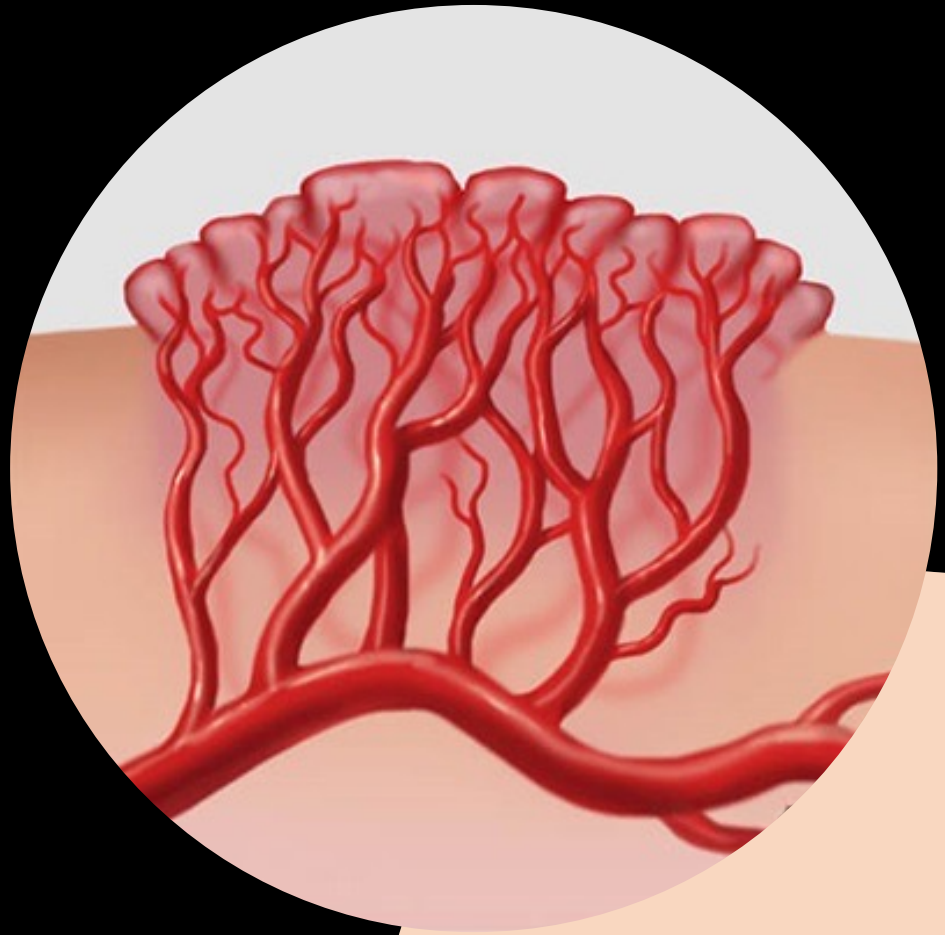
Addressing Thrombosis risk in patients with Vascular Malformations including CLOVES Syndrome.

- VM is NOT infrequent as we used to believe through the last century due to insufficient knowledge of the CVMs as a whole, but VM is rather a common venous disorder

- Indeed, VM is the most common type of the CVMs

- Clarification of Nomenclature
- Special Mention to KTS and PWS
- General Management Directives

Hemangiomas, as vascular tumors have a distinctly different etiology, genetics, presentation, prognosis and treatment.



VM is NOT a Hemangioma

- Most of all, the VM has been wrongly identified as a ‘hemangioma’ for many decades and regretfully still do by many clinicians due to misunderstanding!

Differentiating Features

Hemangioma	Vascular Malformations
•True tumors, with proliferation of the vascular endothelium	•No tumor, Comprised of dysplastic vessels
• >3:1 female:male	•1:1 female:male
•Small or absent at birth	•Present at birth
•Rapid growth during infancy	•Growth proportional to child
•“self-limited”	• never disappear
•Diagnosis:Clinical history+ appearance	•Diagnosis: MRI,Doppler ultrasonography,angiography

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- Multiple nomenclatures → Limited epidemiological data
- The overall incidence of CVMs is now known to be much higher over 1% in general population

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IUA Consensus

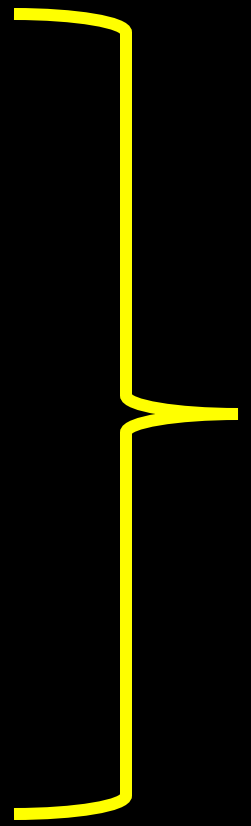
- ***We recommend the preferential use of the modified Hamburg classification of CVMs***

[Strength of recommendation:1 (strong), Quality of evidence: A (high)].

Lee BB, et al International Angiology 2015

Congenital Vascular Malformations

- Arterial (AM)
- Capillary (CM)
- Lymphatic (LM)
- Arterio-Venous (AVM)
- Vascular malformations (VM)
- Combined



CVMs

Hamburg, Germany, 1988

Integrated Classification proposed by IUA Consensus

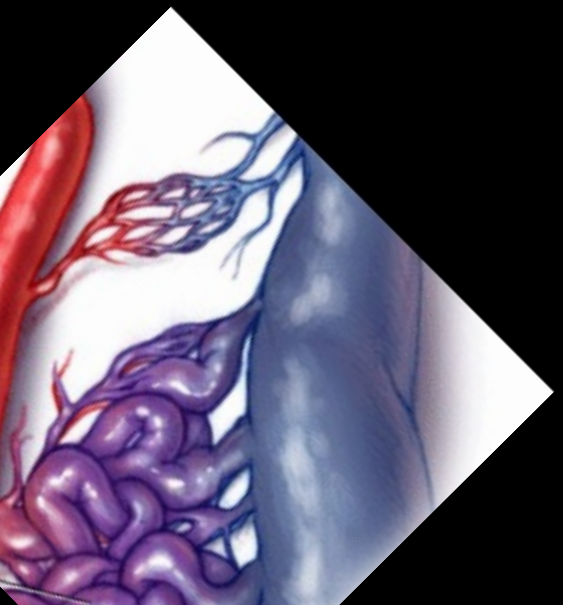
Low Flow			High Flow		
Venous (VM)	Extratruncular	Diffuse/ Infiltrating	Arterial (AM)	Extratruncular	Diffuse/ Infiltrating
		Localized			Localized
	Truncular	Obstruction/ Narrowing		Truncular	Obstruction/ Narrowing
		Dilatation			Dilatation
Lymphatic (LM)	Extratruncular	Diffuse/ Infiltrating	Arterio-venous (AVM)	Extratruncular	Diffuse/ Infiltrating
		Localized			Localized
	Truncular	Obstruction/ Narrowing		Truncular	Obstruction/ Narrowing
		Dilatation			Dilatation
Capillary (CM)					
			Combined		
Syndrome Associated			Syndrome Associated		

Lee BB, et al International Angiology 2015

Klippel-Trenaunay Syndrome (KTS)

Limb overgrowth, nevus and dilated abnormal superficial veins.

The eponym derives from the description of the French authors in 1900, even if similar cases were published earlier by Trelad et Monod in 1869.



Klippel-Trenaunay Syndrome (KTS)

"Typical KTS":

- Cutaneous lesion by CM ("port-wine stain")
- Complex (extratruncular) VM lesion can present as large clusters of abnormal veins throughout the entire extremity, which is infrequently associated with deep vein anomalies
- LM is mostly involved as primary lymphedema
- Limb hypertrophy or gigantism

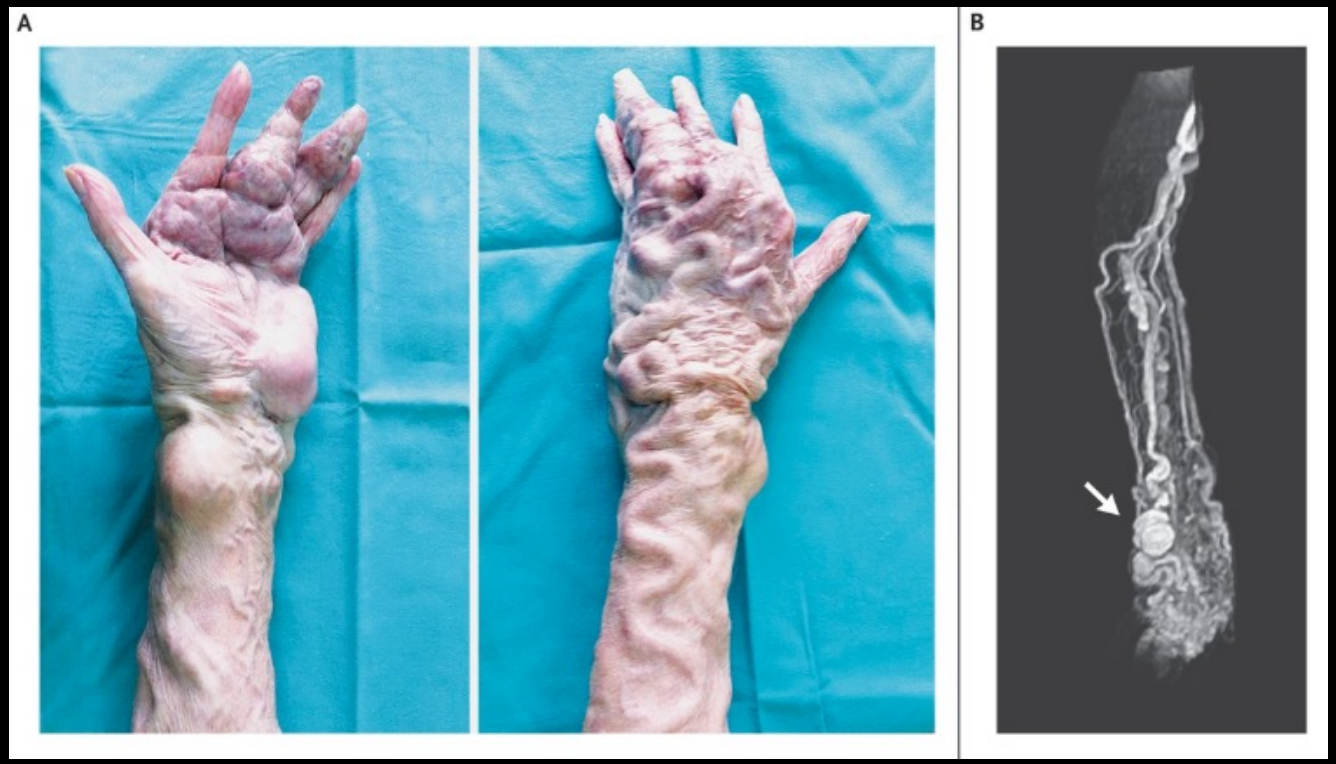
Marginal Vein

- Superficial draining vein of the lower limb which is sited on the lateral edge of the extremity.
- Remnant of an embryonic vessel that normally regresses spontaneously before birth. It is classified as a truncular VM.
- Originates from the superficial compartment, penetrates the deep fascia and involves muscles of the deep compartment.
- Potentially fatal thromboembolic events associated with the MV thrombosis.

www.phlebolymphology.org

Tafur A, Kalodiki E, Fareed J in Controversial issues of the CVM Management. *In Press*

Parkes Weber Syndrome (PWS)

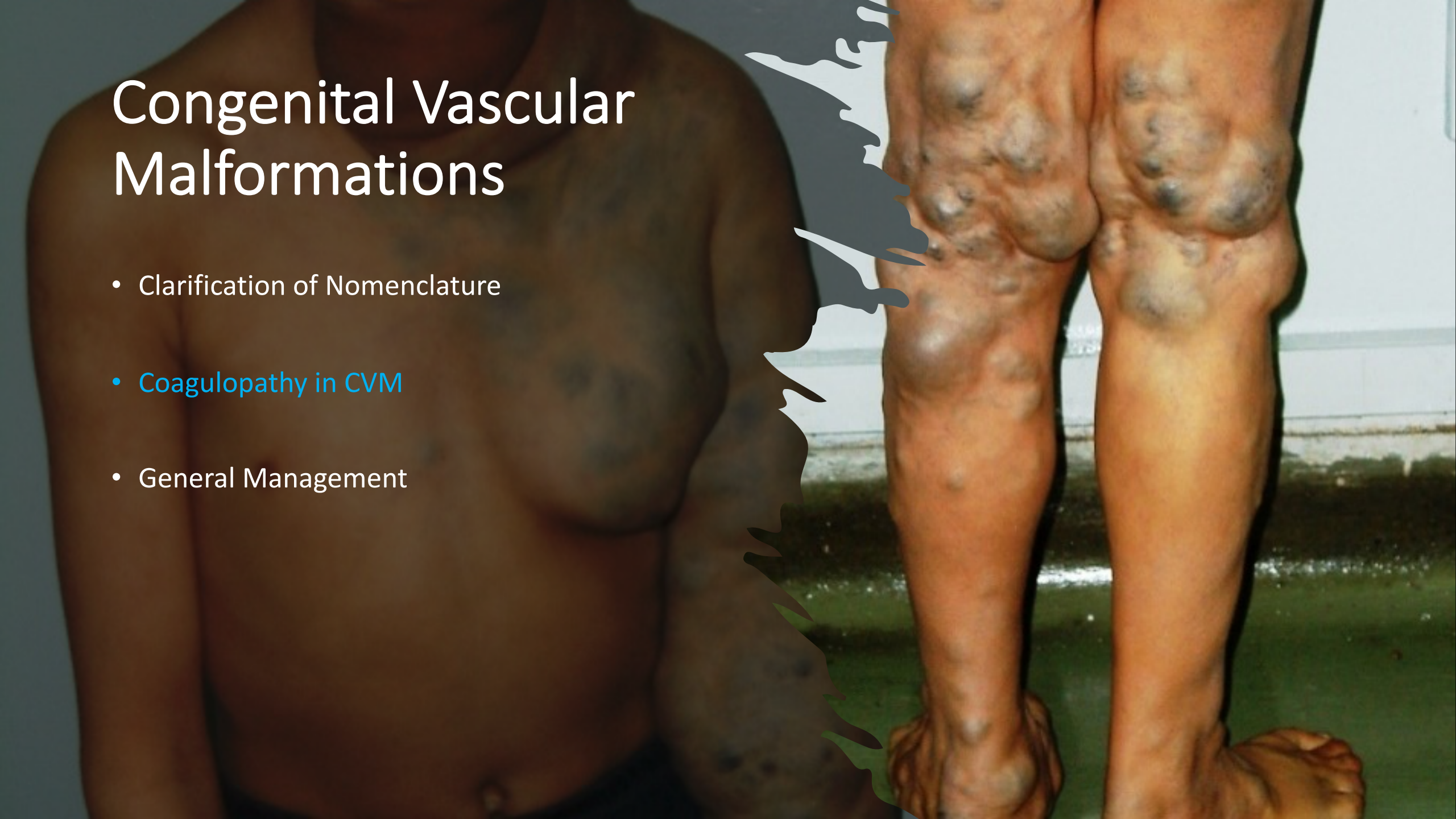


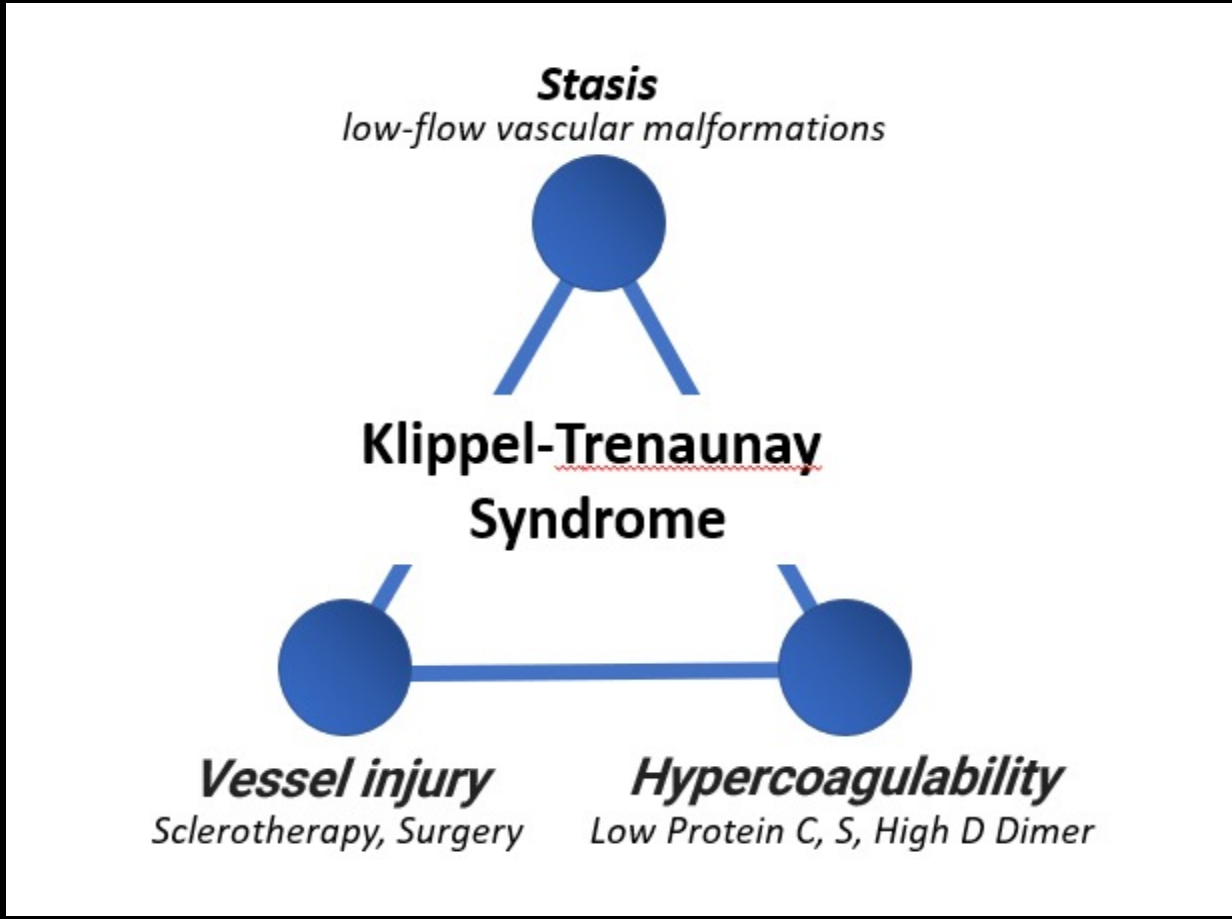
N Engl J Med 2014; 371:2114

- Clinical aspects are similar to KTS with nevus, limb overgrowth and dilated superficial veins.
- However, the main morpho-functional aspect, which differentiates PWS from KTS is the AVM.
- May result from mutations in the RASA1 gene that provides instructions for making a protein known as p120-RasGAP.

Congenital Vascular Malformations

- Clarification of Nomenclature
- Coagulopathy in CVM
- General Management





We recommend a complete thrombophilia workup in patients with a history of thromboembolism or extensive venous malformations (VMs) (surface area > 10 cm, palpable phleboliths)"

[Strength of recommendation:1 (strong), Quality of evidence: C (low)]

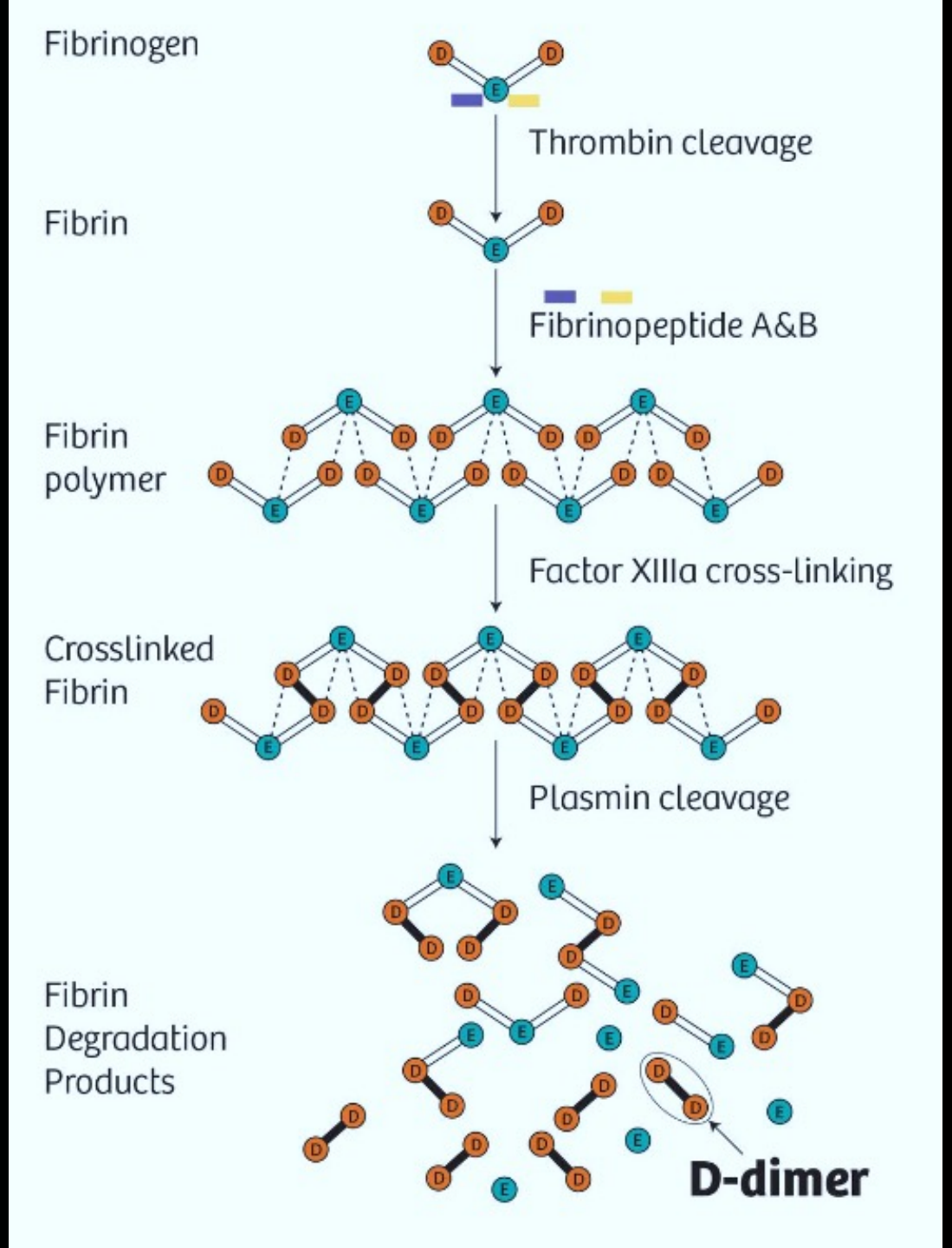
IUA Consensus

Tafur A, Kalodiki E, Fareed J in controversial issues of the CVM Management. *2020*

“Bleeding Disorder “

Initial labs

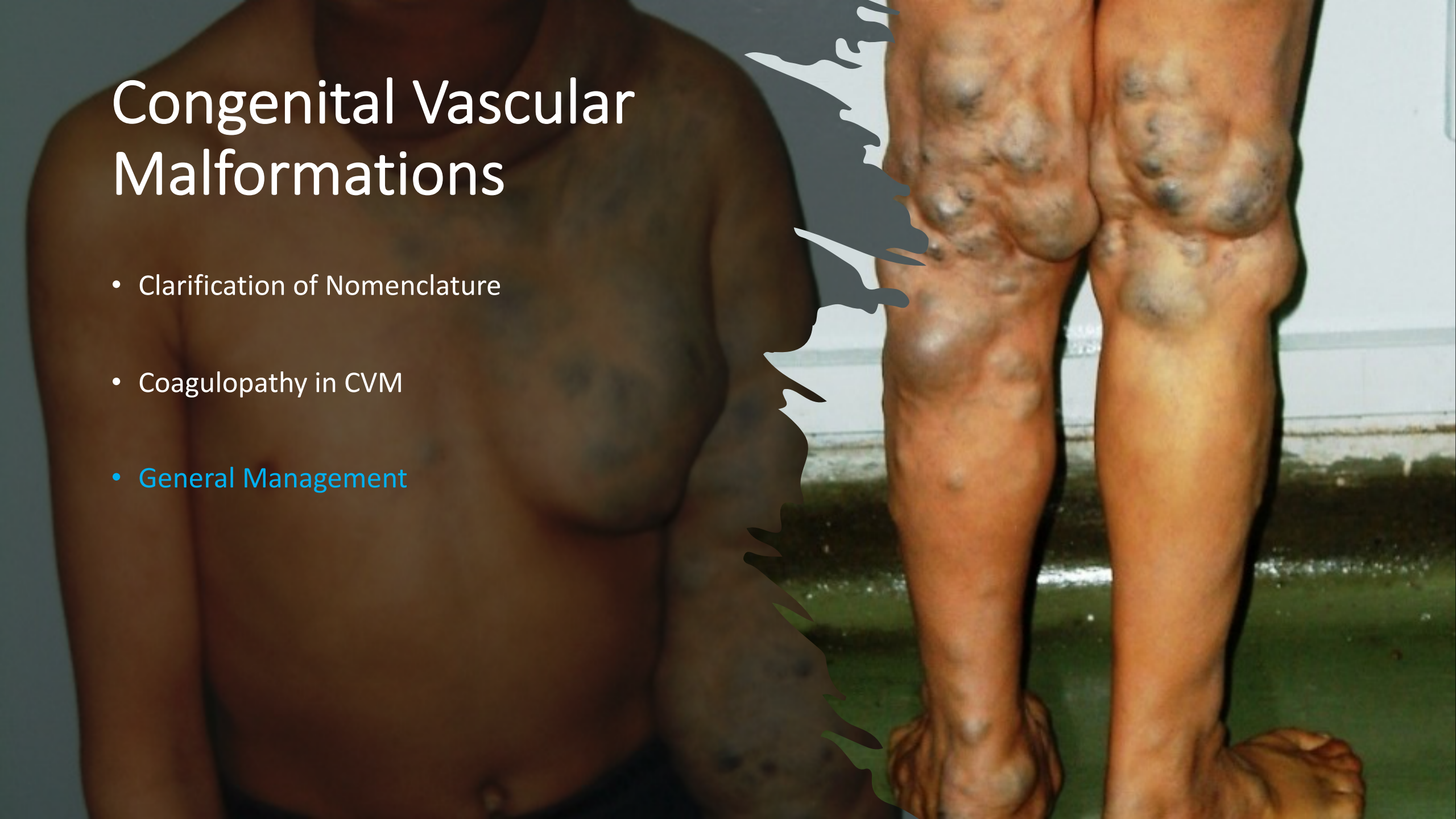
PROTHROMBIN TIME	9.4 - 11.8 s	11.7
INR		1.1
PTT	22 - 30 s	25
FIBRINOGEN	173 - 417 mg/dL	176
D-DIMER ASSAY	***0.00 - 0.49 mgFEU/L***	***14.83 (H)***
FACTOR VIII ASSAY	50 - 150 %	121



PROTHROMBIN TIME	11.3	11.7	11.8	
INR	1.1	1.1	1.2	
PTT	26	25	30	
FIBRINOGEN	120 (L)	119 (L)	107 (L)	204
D-DIMER ASSAY	26.76 (H)	>32.00 (H)		12.55 (H)
FACTOR VIII ASSAY				130

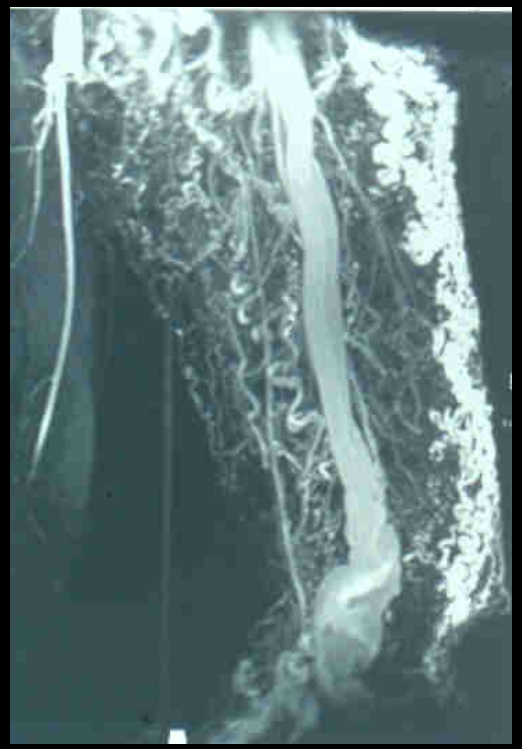
Congenital Vascular Malformations

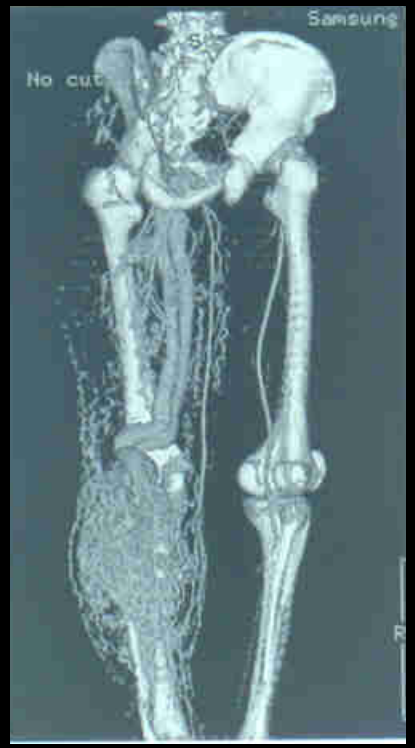
- Clarification of Nomenclature
- Coagulopathy in CVM
- General Management



Conceptual Venous Malformation Management

- Another myth based on limited knowledge on the CVM as a whole is ‘VM and AVM are same! ’ in terms of the care and prognosis, etc. But this is such critical misunderstanding to warrant for the correction because AVM is a potentially limb if not life-threatening condition while the VM in general is NOT.





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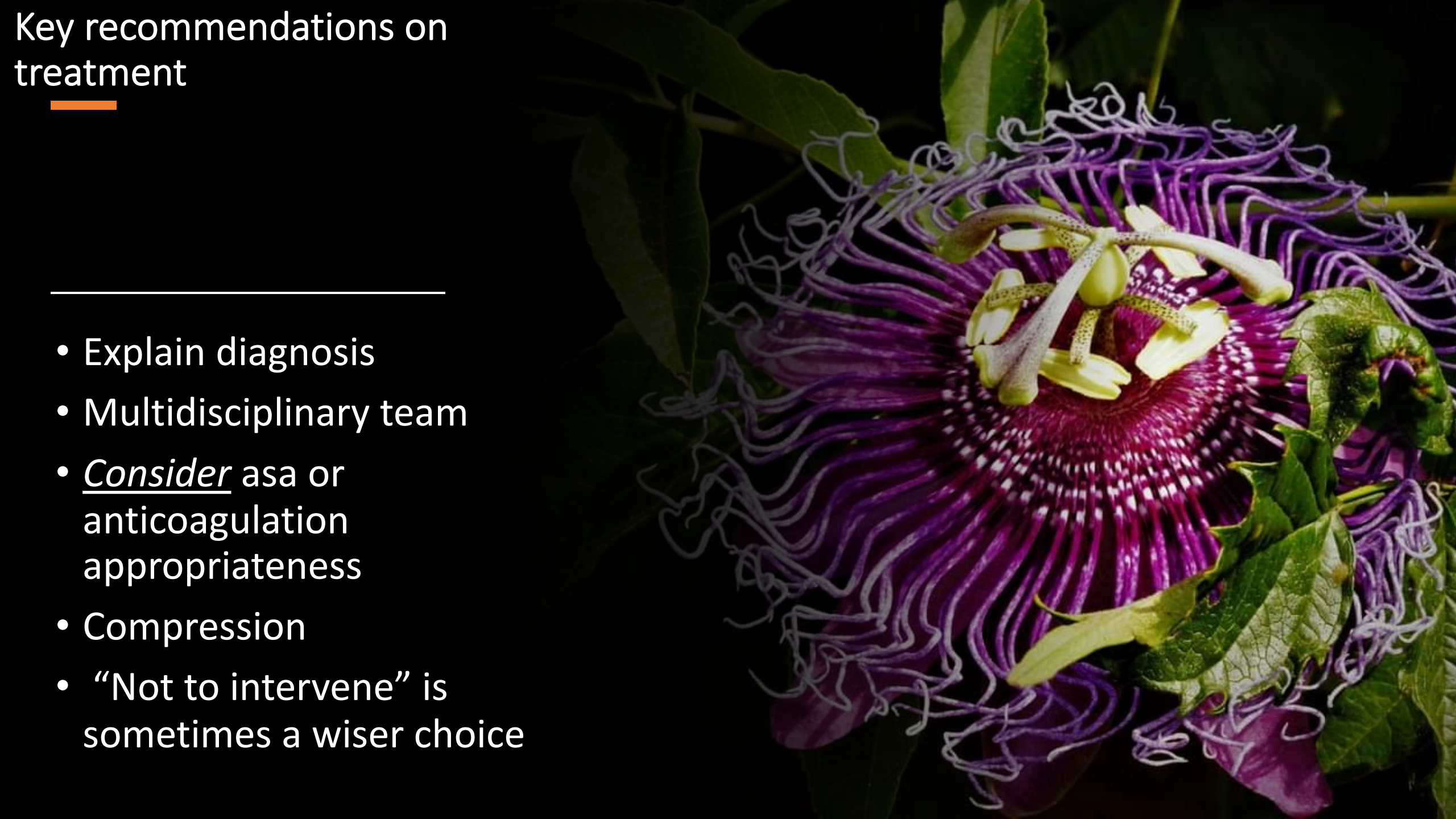
Key recommendations on treatment

- Explain diagnosis
- Multidisciplinary team
- *Consider* asa or anticoagulation appropriateness
- Compression
- “Not to intervene” is sometimes a wiser choice



Thank you

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