Hemostasis

PHYSIOLOGICAL BLOOD CLOTTING IN RESPONSE TO INJURY OR LEAK

no disclosures

Disorders of Hemostasis

- Hemophilia

- von Willebrand Disease

HEMOPHILIA

A defect in the thrombin propagation phase of coagulation

HEMOPHILIA A or B Diagnosis

Bleeding Time	Normal
PT	Normal
APTT	Prolonged
FVIII:c or FIX:c	<1% = severe 1-5% = moderate 6-30% = mild
vWF:Ag	Normal
vWF:Rco	Normal

HEMOPHILIA
Bleeding as a function of clinical severity

Concentration of factor %

50-100:	None
25-50:	Bleeding after sever trauma
6-25:	Severe bleeding after surgery
	Slight bleeding after minor trauma
1-5:	Severe bleeding after slight trauma
<1:	Spontaneous bleeding mainly in joints or muscles

HEMOPHILIA: Clinical features

- Muco-cutaneous bleed
- Hemarthrosis
- Muscle bleeds
- Intra-cranial bleed
- Post-dental bleed
- Post surgical bleed

HEMOPHILIA TREATMENT

- Factor replacement

- DDAVP

- Amicar

- All patients should be cared for life long in bleeding disorder clinic

ACQUIRED HEMOPHILIA CHARACTERISTICS

- AGE: MOST >50

- BLEEDING PATTERN: More severe soft tissue bleed
  hemarthrosis less common

- INHIBITOR

- UNDERLYING DISORDER: usually none, but can be seen post partum, autoimmune disease, malignancy, drug reaction

ACQUIRED HEMOPHILIA

- Major bleeding requiring transfusion: >75%

- Death due to bleeding: >15%

- Immediate Rx with appropriate activated factor products

- Long term: Attempt suppression of inhibitor

VON WILLEBRAND DISEASE

-Most common inherited bleeding disorder presenting with: mucocutaneous bleeds, nosebleeds, bleeding with dental work, heavy menses

- Family history of bleeding

- Decreased levels of VWF

- Autosomal Dominant

- Bleeding usually mild to moderate

VON WILLEBRAND DISEASE

<u>DIAGNOSIS:</u>

- FVIII activity

- VWF antigen

- Ristocetin Cofactor

- PFA

- RIPA

- VWF Multimers

VWH Classification

Type 1: partial quantitative deficiency of VWF

Type 2: qualitative defect in VWF

Type 3: total deficiency of VWF

VWD Classification

TYPE	RIPA	Multimer Pattern	VWF:RCo/Ag
1 Partial Quantitative	decreased or normal	uniform decrease but all present	1:1
Qualitative **2A** **2B**	decreased increased	decrease large multimers decrease large multimers	decreased decreased
2M **2N**	decreased normal	uniform decrease, all present normal multimers	decreased 1:1
3 Severe Deficiency	markedly decreased	Undetectable; usually cannot visualize	N/A

VWD TREATMENT

- DDAVP

- Factor VIII concentrates that contain vWF

- Antifibrinolytics (Amicar, gel foam w/thrombin)

- Severe types should be cared for lifelong at a bleeding disorder center

THROMBOSIS

Pathological Blood Clotting

no disclosures

HYPERCOAGUABLE STAGES

ACQUIRED:

- Advancing age
- Prior thrombosis
- Immobilization
- Major Surgery
- Malignancy
- Estrogens
- Pregnancy
- Trauma
- Paralysis
- Antiphospholipid Antibody Syndrome
- Myeloproliferative disorders
- PNH
- IBD
- Nephrotic syndrome
- HIT
- Prolonged air travel
- Central venous catheters
- Obesity

HYPERCOAGUABLE STAGES

INHERITED:

- **Antithrombin III deficiency 20 fold RR**
- **Protein C deficiency 10 fold RR**
- **Protein S deficiency 10 fold RR**
- **Factor V leiden 3-8 fold RR**
- **Prothrombin gene mutation 3 fold RR**

HYPERCOAGUABLE STAGES: Who to test

Strongly Thrombophylic Clinical History

- **Age of onset <50**
- **Recurrent thrombosis**
- **Positive family h/o thrombosis, MI, CVA at young age**
- **Cerebral venous thrombosis**
- **Portal or mesenteric vein thrombosis (r/o MPD, PHN)**

Consider: VTE associated with OCPs/HRT or pregnancy
Pregnancy loss in 2nd or 3rd trimester

HYPERCOAGUABLE STAGES: Who to not test

- Pts >50 with first spontaneous VTE
- VTE in pts with active cancer
- Elderly pts, especially post-op VTE
- Retinal vein thrombosis
- Arterial thrombosis
- Women starting OTCs with no personal or family history of VTE

HYPERCOAGUABLE WORKUP

- Prothrombin gene mutation
- Factor V Leiden (Activated Protein C resistance)
- Antithrombin III
- Protein C activity
- Protein S assay, total & free
- Tests for antiphospholipid antibody syndrome:
  - Lupus Anticoagulant
  - Anticardiolipin & B2-glycoprotein I antibodies

TREATMENT OF DVT/PE

- HEPARIN
  Unfractionated or LMW for 5 days

- WARFARIN
  Start day 1
  INR 2-3
  Treat 3-6 months

DIRECT ORAL ANTICOAGULANTS

- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)
- KNOW YOUR DRUG

NOACs: When not to use

- Pregnancy associated with VTE
- Cancer associated VTE
- Obese patients (>275 lbs)
- Very frail patient (<100 lbs)
- Renal dysfunction-cr cl <30;
  (use with caution in cr cl 30-40)
- Patients on medicine with major interactions
- Cautious with difficult patients, ie: recurrent DVT/PE on anticoagulation
- Ensure patients comply and can acquire med

DURATION OF ANTICOAGULANT THERAPY

- First isolated, unprovoked distal DVT or proximal DVT/PE secondary to a transient risk factor: 3 months

- Second unprovoked DVT/PE: long-term

- VTE in setting of active cancer: LMWH at least 3 mos vs long-term

DURATION OF ANTICOAGULANT THERAPY

SPECIAL SITUATIONS: Consider indefinite anticoagulation after first event in following cases:

- **Cancer-until resolved (consider LMWH)**
- **Antiphospholipid antibody syndrome**
- **Antithromin III deficiency**
- **Protein C or S deficiencies**
- **Multiple genetic defects**

DURATION OF ANTICOAGULANT THERAPY

Criteria for long term oral anticoagulation:

- **No resolution of triggering risk**
- **Sites and severity of thrombosis**
- **Identification of a prothrombotic defect**
- **Family thrombotic history**
- **Bleeding risk**
- **Patient preference (life style, occupation) with understanding of risks vs. benefits**

THANK YOU!

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