Bleeding and Thrombotic Disorders

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Bleeding and Thrombotic Disorders

Bleeding disorders
• von Willebrand disease
• Hemophilia
• DIC
• TTP/HUS

Thrombotic disorders
• Factor V Leiden
Bleeding symptoms depend (somewhat) on underlying cause!

“Platelet” bleeding
- Superficial (skin)
- Petechiae
- Spontaneous

“Factor” bleeding
- Deep (joints)
- Big bleeds
- History of trauma *

* Includes prolonged bleeding after dental work
Petechiae vs. purpura
Bleeding and Thrombotic Disorders

Bleeding disorders
  • von Willebrand disease
Von Willebrand Disease

Things you must know

- Most common hereditary bleeding disorder
- Autosomal dominant
- vW factor decreased (or abnormal)
- Variable severity
What’s von Willebrand Factor?

- Huge multimeric protein
- Made by megakaryocytes and endothelial cells
- Two functions:
  - Glues platelets to subendothelium
  - Carries factor VIII (prevents its degradation)
vWF is the “glue” that sticks platelets to subendothelial proteins
vWF also carries FVIII, preventing it from degrading.
Symptoms of Von Willebrand Disease

- Mucosal bleeding in most patients (due to decreased platelet adhesion)
- Deep joint bleeding in severe cases (due to decreased fibrin formation)
Von Willebrand Disease

Diagnosis
• Bleeding time: prolonged
• PTT: prolonged (in severe cases)
• PT/INR: normal

Treatment
• Desmopressin (↑ release of vWF and VIII)
• Cryoprecipitate (contains vWF and VIII)
Bleeding and Thrombotic Disorders

Bleeding disorders
  • von Willebrand disease
  • Hemophilia
Hemophilia

Things you must know

• Most common factor deficiency

• X-linked recessive in most cases (30% are spontaneous mutations)

• Hemophilia A = ↓ VIII (more common)
  Hemophilia B = ↓ IX

• Variable amount of “factor” bleeding
Hemophilia A

Hemophilia B

**Intrinsic**

- IX
- VIII
- V

**Extrinsic**

- TF VII

Thrombin → Fibrin
Hemophilic arthropathy of knee

Normal knee

Knee of patient with hemophilia

Hemophilic arthropathy of knee
Joint deformity in hemophilia
Hemophilia

Diagnosis
- PTT: prolonged
- PT/INR: normal
- Bleeding time: NORMAL!

Treatment of hemophilia A
- Desmopressin
- Recombinant Factor VIII

Treatment of hemophilia B
- Recombinant Factor IX
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Disseminated Intravascular Coagulation (DIC)

Things you must know

- Excessive clotting and bleeding
- Many potential causes
- Blood: MAHA and thrombocytopenia
- PT/INR, PTT, and bleeding time prolonged
What’s going on in DIC?
Symptoms of DIC

Thrombosis

Hemorrhage
Remember these causes of DIC:

- Malignancy
- OB complications
- Sepsis
- Trauma
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Thrombotic Thrombocytopenic Purpura/Hemolytic-Uremic Syndrome

Things you must know

• Both have widespread clotting (± bleeding)
• Cause: ADAMTS13 deficiency (TTP) or E. coli (HUS)
• Symptoms: renal failure, neurologic symptoms
• Coagulation factors (and tests) are normal!
Deficiency of ADAMTS 13 in TTP
Nasty creatures in TTP

Rodent of unusual size (ROUS)
- *The Princess Bride*, 1987

Von Willebrand multimer of unusual size (MOUS)
- *NEJM*, 1982
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Thrombotic disorders
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Thrombosis Risk Factors

Endothelial damage
• Atherosclerosis

Stasis
• Immobilization
• Varicose veins
• Cardiac dysfunction

Hypercoagulability
• Surgery
• Carcinoma
• Estrogen/postpartum
• Thrombotic disorders
When should you worry about a hereditary disorder?

- no obvious cause
- family history
- weird location
- recurrent
- patient is young
- miscarriages
Most common cause of unexplained thromboses
Inherited point mutation in factor V gene
Mutated factor V can’t be turned off!
Diagnosis requires genetic testing
Intrinsic

Extrinsic

[Diagram: Diagram showing the intrinsic and extrinsic coagulation pathways.]

- IX
- VIII
- V
- X

TF VII

Thrombin

Fibrin
Intrinsic

IX

VIII

V

Va

protein C

Extrinsic

TF VII

X

thrombin

fibrin
Intrinsic

- IX
- VIII
- V Leiden → VLa
- protein C

Extrinsic

- TF VII
- X
- thrombin
- fibrin
Factor V Leiden

Diagnosis
• PT/INR and PTT: normal!
• Need genetic testing

Treatment
• Don’t! Unless there is a thrombosis.
• Then give oral anticoagulants