Bleeding and Thrombotic Disorders

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Bleeding and Thrombotic Disorders

Bleeding disorders
- von Willebrand disease
- Hemophilia A and B
- DIC
- TTP/HUS
- ITP

Thrombotic disorders
- Factor V Leiden
Platelet bleeding
• Superficial (skin)
• Petechiae
• Spontaneous

Factor bleeding
• Deep (joints)
• Big bleeds
• Trauma *

* Includes prolonged bleeding after dental work
Petechiae
Palatal petechiae
Palatal ecchymosis
Bleeding after buttock injection in patient with hemophilia
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 megs and endothelial cells
• Glues platelets to endothelium
• Carries factor VIII
• Decreased or abnormal in vW disease
Extrinsic coagulation sequence

Exposure of membrane-bound tissue factor

Platelet adhesion: Held together by fibrinogen

vWF

Collagen
Thrombin

fibrin

clot

Intrinsic

Extrinsic

TF VII

V

X

IX

VIII
Symptoms of Von Willebrand Disease

- Mucosal bleeding in most patients
- Deep joint bleeding in severe cases
Lab Tests in Von Willebrand Disease

- Bleeding time: prolonged
- PTT: prolonged (‘corrects’ with mixing study)
- PT: normal
Treatment of Von Willebrand Disease

- DDAVP (raises VIII and vWF levels)
- Cryoprecipitate (contains vWF and VIII)
- Factor VIII
Bleeding disorders

- von Willebrand disease
- Hemophilia A and B
Hemophilia A

Things you must know

- Most common factor deficiency
- X-linked recessive in most cases (30% are spontaneous mutations)
- Factor VIII level decreased
- Variable amount of “factor” bleeding
Intrinsic

IX

Extrinsic

TF VII

VIII

V

thrombin

fibrin

clot
Hemophilic arthropathy of knee

Normal knee  Knee of patient with hemophilia

Hemophilic arthropathy of knee
Joint Deformity in Hemophilia
Hemophilia A

Lab tests
- PTT prolonged
- Factor VIII level low
- DNA studies abnormal

Treatment
- DDAVP
- Factor VIII
Hemophilia B

Things you must know

- Factor IX level decreased
- Much less common than hemophilia A
- Same inheritance pattern
- Same clinical and laboratory findings
Intrinsic

IX

VIII

Extrinsic

TF VII

X

V

thrombin

fibrin

clot
Bleeding and Thrombotic Disorders

Bleeding disorders

- von Willebrand disease
- Hemophilia A and B
- DIC
Thrombosis

Hemorrhage
Remember these for sure:

- Malignancy
- OB complications
- Sepsis
- Trauma
Bleeding and Thrombotic Disorders

Bleeding disorders

- von Willebrand disease
- Hemophilia A and B
- DIC
- TTP/HUS
Thrombotic Thrombocytopenic Purpura

Things you must know

- Pentad: MAHA, thrombocytopenia, fever, neurologic defects, renal failure
- Deficiency of ADAMTS13
- Big vWF multimers trap platelets
- Plasmapheresis or plasma infusions
Cleaved unusually large multimers of von Willebrand factor

ADAMTS 13

Endothelial cell

Secretion of multimers from Weibel-Palade body

Adhesion and aggregation of platelets

Uncleaved unusually large multimers of von Willebrand factor

ADAMTS 13

Endothelial cell

Secretion of multimers from Weibel-Palade body
Nasty creatures

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

Von Willebrand multimer of unusual size (MOUS)
- *NEJM*, 1982
Thrombotic Thrombocytopenic Purpura

Clinical pentad

- Hematuria/jaundice (MAHA)
- Bleeding/bruising (thrombocytopenia)
- Fever
- Bizarre behavior (thrombi in CNS)
- Renal failure (thrombi in kidney)

Treatment

- Plasmapheresis (in acquired TTP)
- Plasma infusions (in hereditary TTP)
Hemolytic Uremic Syndrome

Things you must know

- MAHA and thrombocytopenia
- Most are related to E. coli infection
- Toxin damages endothelium
- Treat supportively
Bleeding and Thrombotic Disorders

Bleeding disorders
  • von Willebrand disease
  • Hemophilia A and B
  • DIC
  • TTP/HUS
  • ITP
Idiopathic Thrombocytopenic Purpura

Things you must know

- Antiplatelet antibodies coat platelets
- Splenic macrophages eat platelets
- Diagnosis of exclusion
- Steroids or splenectomy
Bleeding and Thrombotic Disorders

Bleeding disorders
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- DIC
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Thrombotic disorders
- Factor V Leiden
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
Factor V Leiden

Things you must know

- Most common cause of unexplained thromboses
- Inherited point mutation in factor V gene
- Factor V can’t be turned off
- High risk of thrombosis if homozygous
What is Factor V Leiden?

A mutated factor V gene
• Single point mutation
• Discovered in Leiden, Netherlands

Produces abnormal factor V
• Participates in the cascade
• Can’t be cleaved by protein C
You can turn it on...

...but you can’t turn it off!
Factor V Leiden

**Diagnosis**
- PTT and INR not helpful
- Need genetic testing

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