Approach to the bleeding patient

Michael B Streiff, MD FACP
Associate Professor of Medicine and Pathology
Medical Director, Johns Hopkins Anticoagulation Service
Johns Hopkins Medical Institutions

Disclosures

• No relevant disclosures

Hemostasis

Vessel wall
Platelets
Coagulation proteins
Platelet structure

The Coagulation Cascade

Drawings courtesy Thomas S Kickler, MD
The Fibrinolytic System

- Plasminogen
- TPA
- UK
- Plasmin
- α2-antiplasmin
- Fibrinogen
- FDP
The Bleeding History

- Spontaneous
- Frequency
- Severity
  - Physician visit
  - Medications
  - Emergency Department
  - Transfusion
  - Surgery
  - Epistaxis
    - > 15 minutes
    - Cautery
    - Transfusion
    - Hospital stay
  - Hemarthrosis
  - Dental surgery
    - Bleed > 24 hrs.

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The Bleeding History

- Menorrhagia
  - Duration > 7 days
  - Change lifestyle
- Bruises
  - Size > 6 cm
  - Spread with gravity
- Wound healing difficulties

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The Bleeding History

- Congenital or acquired?
  - Circumcision
  - Menstruation
  - Epistaxis
  - Tonsillectomy
  - Wisdom tooth extraction
- Medications- NSAIDS, Aspirin, Vitamins, Supplements
The Bleeding History

- Platelet Bleeding
  - Mucosal bleeding
    - Epistaxis (nose bleeds)
    - Dental bleeding
    - Gastrointestinal bleeding
    - Menorrhagia (heavy periods)
- Coagulation Factor Bleeding
  - Hemarthrosis (joint bleeds)
  - Deep muscle/tissue bleeds
- Fibrinolytic or Factor XIII defect
  - Delayed bleeding

Bleeding Medical History

- Kidney disease
  - Platelet defect
- Liver Disease
  - Thrombocytopenia, factor deficiency, fibrinolysis
- Malabsorption/malnutrition
  - Factor deficiency
- Autoimmune disease (SLE, Thyroid disease)
  - Thrombocytopenia, platelet dysfunction, factor inhibitors

Bleeding Medical History

- Lymphoproliferative diseases (Chronic Lymphocytic leukemia, Lymphoma)
  - Thrombocytopenia, Factor inhibitors, von Willebrand disease
- Myeloproliferative neoplasms
  (Polycythemia vera, essential thrombocythemia)
  - Platelet dysfunction, von Willebrand disease, thrombocytopenia
Bleeding Medical History

- Acute Leukemia –
  - Thrombocytopenia, Disseminated intravascular coagulation
- Myeloma -
  - Thrombocytopenia, platelet dysfunction, fibrin polymerization defect
- Amyloid
  - Factor deficiency, vascular fragility

Family History

- Sex-linked recessive inheritance
  - Hemophilia A (Factor 8 deficiency)
  - Hemophilia B (Factor 9 deficiency)
- Autosomal dominant
  - Von Willebrand disease
  - Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu)
- Autosomal recessive
  - Factor deficiencies
  - Type 3 von Willebrand disease
  - Platelet dysfunction (Bernard-Soulier, Glanzmann’s thrombasthenia, gray platelet syndrome)

Physical Examination

- Systemic versus local defect
  - One site versus many sites
  - Rapid versus slow
- Petechiae = platelets
- Mucous membrane = platelets

Physical Examination

- Hemarthrosis = factor deficiency
- Massive hematoma = Factor 8 inhibitor
- Joint laxity, skin elasticity, "tissue paper" skin = Ehlers-Danlos

Physical Examination

- Peri-follicular hemorrhages, corkscrew hairs = scurvy
- Telangiectasias = Osler-Weber-Rendu (HHT)

Petechiae or telangiectasias?

Acquired Bleeding Disorders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Signs/Symptoms</th>
<th>Confirmatory test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired Factor 8 inhibitor</td>
<td>Soft tissue hematoma</td>
<td>Factor 8 activity, Factor 8 inhibitor assay</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Soft tissue hematoma, bruises</td>
<td>Factor levels, Fat pad biopsy</td>
</tr>
<tr>
<td>DIC/Fibrinolysis with acute leukemia</td>
<td>Multiple ecchymoses</td>
<td>Prolonged PT, aPTT, low fibrinogen, Elevated DD</td>
</tr>
<tr>
<td>Factitious purpura</td>
<td>Unusual bruises, purpura</td>
<td>Normal labs</td>
</tr>
<tr>
<td>Scurvy</td>
<td>Perifollicular bleeding, bruises</td>
<td>Dietary history, Normal platelets, Low Vitamin C</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Petechiae</td>
<td>Low platelet count</td>
</tr>
<tr>
<td>Vitamin K deficiency</td>
<td>Soft tissue bleeds, ecchymoses, hematuria</td>
<td>Prolonged PT, aPTT, poor diet</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Soft tissue bleeds, ecchymoses, hematuria</td>
<td>Prolonged PT, aPTT,</td>
</tr>
</tbody>
</table>

Bleeding and the prolonged PT

- Inherited or acquired?
- Deficiency
  - Vitamin K deficiency
  - Warfarin
  - Liver disease
  - Factor VII deficiency
- Inhibitor
  - Factor VII inhibitor

Bleeding and the prolonged aPTT

- Inherited or acquired
- Deficiency
  - Intrinsic Factor deficiency
  - Von Willebrand disease
  - Liver disease
- Inhibitor
  - Anticoagulant (Heparin, etc)
  - Factor Inhibitor
Bleeding and a normal aPTT and PT

- Platelet disorder
  - Thrombocytopenia
  - Platelet dysfunction
- Von Willebrand disease
- Factor XIII deficiency
- Fibrinolytic defect
- Vascular Defect
- Factor XIV deficiency

Coagulation Disorders

- Prolonged PT
  - Vitamin K
  - Prothrombin complex concentrates
  - FFP
- Prolonged aPTT
  - Factor concentrates
  - FFP
  - Protamine
  - aPCC
- Normal PT and aPTT
  - Platelet disorder RX
  - Von Willebrand RX
  - FFP (factor XIII)
  - Anti-fibrinolytic (fibrinolytic defect)
  - Ehlers-Danlos- DDAVP, anti-fibrinolytic
  - Factor XIV- surgeon

Von Willebrand disease

- vWF Function:
  1. Platelet adhesion
  2. FVIII protection
- Autosomal dominant/recessive, 1/5000
- Mucocutaneous bleeding
vWD: Diagnosis

- Bleeding history
- APTT: insensitive
- Platelet Count
- PFA 100
- Factor VIII activity
- Ristocetin cofactor activity
- vWF antigen
- vWF multimers
- Platelet aggregometry

vWD: Treatment

- Determine vWD type
- Determine DDAVP responder status
- Treatment
  - Type 1- DDAVP, Anti-fibrinolytics, Factor 8 concentrates
  - Type 2- Factor 8 concentrates, Anti-fibrinolytics, DDAVP
  - Type 3- Factor 8 concentrates, Anti-fibrinolytics

Quantitative Platelet Disorders

Production: B12/Folate, Bone marrow disease, Drugs, Liver disease, Infections
Destruction: Drugs, Infections, ITP, TTP/HUS, DIC
Sequestration: Hypersplenism
Qualitative Platelet Disorders

- Congenital - Bernard-Soulier Syndrome, Glanzmann's Thrombasthenia, Storage Pool Disease
- Acquired - Drugs, Renal failure, Myeloproliferative disorders

Quantitative Platelet Disorders

- CBC
- Peripheral smear
- Immature Platelet Fraction
- HIT ab testing
- Bone marrow
- Platelet ab testing

Qualitative Platelet Disorders

- CBC
- Peripheral smear
- Bleeding Time
- APTT, VWF antigen, Ristocetin Cofactor assay, VWF multimers
- Platelet Aggregation
- Flow cytometry
- Electron microscopy
Treatment of Bleeding Disorders

- Thrombocytopenia
  - Cause specific therapy
- Platelet dysfunction
  - DDAVP
  - Platelet transfusions
  - Anti-fibrinolytic agents
  - rhFVIIa

Vascular Disorders

- Scurvy
- Amyloid
- Old age
- Steroids
- Connective Tissue Disorder
- Vasculitis

The evaluation of the bleeding surgical patient

- Assess the clinical features of the bleeding
- Review pre-op history and labs
- Review pre-op and intra-op meds and blood products
- Repeat labs (CBC, Smear, PT, aPTT, Thrombin time, D-dimer)
Post-procedure Bleeding: Causes

- Early Bleeding
  - Surgical Bleeding
  - Quantitative or qualitative platelet disorders
    - Thrombocytopenia
    - NSAIDs/ASA/Supplements
    - Congenital/acquired platelet dysfunction
  - Von Willebrand Disease
    - Congenital
    - Acquired- Heyde’s syndrome, Myeloproliferative neoplasms, Lymphoproliferative disease, Autoimmune diseases

- Thrombocytopenia

- NSAIDS/ASA/Supplements

- Congenital/acquired platelet dysfunction

- Von Willebrand Disease

- Early Bleeding
  - Coagulation disorders
    - Hemophilia and other congenital factor deficiency
    - Acquired factor deficiency- factor inhibitors, DIC
    - Anticoagulation
  - Delayed Bleeding
    - Excessive fibrinolysis
      - Congenital or acquired
    - Factor XIII deficiency
    - Vitamin K deficiency
    - Anti-thrombotic therapy

Questions?