Bleeding Disorders in Pediatrics
David Ungar MD

Disclosures
- Novo Nordisk – consultant
- ICON Clinical Research - employee

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Case #1
A 2 year old female is brought to the office with a one day history of easy bruising. She has been previously well. The child has multiple bruises on examination and bilateral periorbital ecchymoses. How will you evaluate and manage this child?

What Labs Would You Order?
- Order CBC, PT, PTT
- PT, PTT normal,
- CBC shows profound thrombocytopenia with other cell lines normal

**DIAGNOSIS:**
Immune Thrombocytopenic Purpura (ITP)

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**Evaluating The Bleeding Child**

- **History**
  - bleeding - site, frequency, duration, association with trauma, onset
  - PMH, previous surgery, medications, family history
- **Physical**
  - Signs of bleeding - bruises, petechiae, hemarthrosis
  - Evidence of chronic bleeding and stigmata of other disorders

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**bruises on legs**
Screening Laboratory Evaluation
- CBC, platelet count, review smear
- PT, PTT
- Bleeding time should not be part of routine evaluation
- Platelet count, PT, PTT are generally adequate to rule out clinically significant bleeding disorders in asymptomatic children

Platelet Disorders
- Quantitative
  - ITP
  - Marrow Failure (infection, aplastic anemia, drugs)
  - Marrow Infiltration (leukemia)
- Qualitative
  - Platelet Function Disorders
  - Drugs

Immune Thrombocytopenic Purpura (ITP)
- Incidence 32/million children less than 15
- Peak at age 2-5 years, smaller peak in teens
- Platelet autoantibodies probably produced in response to a viral trigger
- Presents with sudden onset of petechiae, purpura, or other bleeding
- Platelet count commonly <20,000
Immune Thrombocytopenic Purpura (ITP)

- 90% will recover spontaneously within 6 months
- Treatment options
  - Observation
  - IVIG
  - IV anti-D
  - Corticosteroids (consider bone marrow first)
- 10% will be chronic; require more specialized management

Case #2

A nine month old Vietnamese male is brought to the ER by his mother because he has a large hematoma on the side of his head. Her English is limited, but she says she doesn’t know how this happened. The ER physician notes multiple bruises in various stages of healing and is concerned about child abuse, so you are called for a consult.
What Labs Would You Order?

Order PT, PTT, CBC
PT, platelet count normal
PTT is 70

What is the Next Step?
• Order Factor VIII and IX
• Factor VIII is less than 1%

DIAGNOSIS: Hemophilia A

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Hemophilia

- Deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B)
- X-linked recessive inheritance
- Will have prolonged PTT; diagnosis by specific factor levels

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Hemophilia

- Severity of bleeding based on factor levels
- Most severe and moderate patients will have joint bleeding
- CNS, airway, and exsanguinating bleeds may be life-threatening
- Therapy involves prompt specific factor replacement
Factor VIII Deficiency

- Estimated 1 in 5,000 to 1 in 10,000
- Classified as mild, moderate, and severe based on factor VIII level
  - <1% is severe (50% of patients)
  - 1-5% is moderate (10% of patients)
  - >5% is mild (40% of patients)
- 1/3 of cases have no family history (new mutation)

Factor IX Deficiency

- Estimated 1 in 25-50,000
- Classified as mild, moderate, and severe based on factor IX level (similar to FVIII)

Clinical Presentation and Diagnosis

- 2/3 of patients will be diagnosed by testing based on a positive family history
- Other children will present with bruising or bleeding
- Only 30% will bleed with circumcision
Therapy of Hemophilia A

- All severe patients and most moderate patients need factor concentrate
- Most people use recombinant Factor VIII
- Virally-inactivated plasma derived products are also acceptable
- Cryoprecipitate should not be used except in life-threatening situations when no other product is available
- Mild patients may be treated with DDAVP

DDAVP for Hemophilia A

- Will increase FVIII levels 2 to 3 fold
- Should be used only in patients known to be DDAVP responsive
- Should not be used for potentially life-threatening bleeds
- Available as IV or nasal form (Stimate)
  - IV 0.3 mcg/kg in 50 ml NS over 30 minutes
  - Nasal 1 puff in 1 nostril (<50 kg) or 1 puff in each nostril (>50 kg)

DDAVP for Hemophilia A

- Hyponatremia may be a problem, especially in infants. May see flushing and headache
- Patients should be instructed to avoid excessive fluid intake (drink no more than a normal amount)
Therapy of Hemophilia B

- Most people use recombinant Factor IX
- Virally-inactivated plasma derived products are also acceptable
- Recombinant Factor IX has different kinetics in young children, may require higher doses
- DDAVP and cryoprecipitate do not work for Hemophilia B
- Fresh frozen plasma may be used in life-threatening bleeding if factor concentrate unavailable

Prophylaxis

- Use of prophylactic factor VIII (3X/wk) or IX (2x/wk) has been shown to decrease the incidence of chronic joint disease in children with severe hemophilia
- Tailored Prophylaxis
  - Start with one treatment a week, increase frequency if has breakthrough bleeding
  - May avoid port
  - Potentially less costly

Low Level Carrier

- Results from unbalanced Lyonization
- May have factor levels in the mild hemophilia range
- Clinical symptomatology similar to mild hemophilia.
- May also have menorrhagia
Obstetrical Management

- Mother known carrier or positive family history and carrier status unknown
  - No vacuum extraction or high forceps
  - If newborn is male, send cord blood factor VIII or IX
  - No circumcision until factor level known

The Future

- Gene Therapy
  - Gene for factor VIII and IX have both been cloned
  - Gene therapy will most likely convert patients with severe hemophilia to moderate hemophilia
  - Several technical factors still to be worked out

The Future

- Bioengineering The Factor Molecule
  - Improved expression (pig milk)
  - Reduce inactivation
  - Reduce clearance
  - Several modified factor VIII and IX products are now in clinical trials
Other Factor Deficiencies

- Fibrinogen (Factor I)
- Prothrombin (Factor II)
- Factor V
- Factor VII
- Factor X
- Factor XI (Hemophilia C)
- Factor XIII

Urgent Therapy of Other Factor Deficiencies

- Hypofibrinogenemia – cryoprecipitate or fibrinogen concentrate
- Prothrombin deficiency – FFP
- Factor V deficiency – FFP
- Factor VII deficiency – rFVIIa 20-25 mcg/kg q6h
- Factor X deficiency – FFP
- Factor XI deficiency – FFP
- Factor XIII deficiency – FFP or factor XIII concentrate
You are seeing a 5 year old male with severe iron deficiency anemia. Patient has persistent anemia despite adequate iron supplementation. On further questioning, the mother states that the child has frequent nosebleeds.

What Labs Would You Order?

- CBC shows hemoglobin of 10, MCV 72
- PT and aPTT are normal
What is the Next Step?

- Order von Willebrand work-up
- Ristocetin Cofactor 0.23, Antigen 25%

DIAGNOSIS: von Willebrand Disease

Further Evaluation of the Child with Bleeding

- For symptomatic children with normal screening labs, consider:
  - Von Willebrand disease
  - Platelet function disorders
- These patients may benefit from referral to a pediatric hematologist.
Von Willebrand Disease

- Most common inherited bleeding disorder, may be as high as 1 in 200
- Quantitative (Type 1) or qualitative (Type 2) defect in von Willebrand factor
- Usually mild, but may be severe (Type 3)
- Usually autosomal dominant inheritance, but may be recessive

History

- First described in 1926 by Dr. Erich von Willebrand
- Severe bleeding in a large family from Foglo in the Aaland islands off the coast of Finland
- Initially called pseudohemophilia, then vascular hemophilia
- Von Willebrand factor described in the 1970’s
- Gene cloned in the 1980’s

Von Willebrand Disease
Clinical Presentation and Diagnosis

- Bruising, mucous membrane bleeding, menorrhagia
- PTT, bleeding time may be normal
- Careful family history important
- Diagnosis by measurement of von Willebrand factor antigen and activity
- Von Willebrand factor is an acute phase reactant, so may get false negatives in patients who are ill, pregnant, or have recent trauma
Therapy of von Willebrand Disease

- Usually mild bleeding
- DDAVP for Type 1, some type 2. Dosing same as for hemophilia.
- Contraindicated in type 2b
- Use intermediate purity factor VIII concentrate (Alphanate, Humate P, Wilate) for Type 2 and 3

Acute Management

General Principles

- First aid is still first aid
- Pressure for epistaxis and cuts
- Rest, compression, elevation for musculoskeletal bleeds
- Ice frequently recommended for acute bleeding, but no clear evidence of clinical benefit
- Specific therapy determined by patient’s underlying disorder and past response to treatment
Head Injury
- Assess mechanism of injury and current patient symptoms
- Patients with symptoms should be seen immediately
- If clinical history and exam are suspicious for intracranial hemorrhage, administer appropriate hemostatic therapy before obtaining imaging
- Patients who are asymptomatic may need to be seen depending on mechanism of injury
- All hemophilia patients who are seen should receive a 100% dose of factor

Joint Bleeding
- Assess whether the bleed is associated with trauma or spontaneous
- Give 60% dose of factor
- Rest, ice, compression, elevation
- Activity should be restricted until pain free and well
- Trauma associated bleeds often require multiple treatments

Soft Tissue Hemorrhage
- Assess for pain, progression, impairment of function as indications for the necessity of treatment
- Size of bruise or hematoma is less important in assessing need for treatment
- Give appropriate activity restrictions based on location of bleed
Epistaxis
- Direct pressure for a minimum of 5 minutes
- If ineffective, can use a cotton ball soaked with oxymetazoline (Afrin) nasal spray to pack nose
- Salt pork can also be used for local hemostasis
- If above measures do not work, consider factor or DDAVP
- Aminocaproic acid (50 mg/kg/dose qid) may be useful in some patients

Oral Bleeding
- Usually seen with trauma
- May see oozing after losing teeth
- Pressure when possible
- No bottle
- Biting on a teabag may help
- Aminocaproic acid swish and swallow qid
- Refractory bleeding may require specific hemostatic therapy

Menorrhagia
- May range from mild to severe enough to require transfusion
- Hormonal therapy is usually first line
- Aminocaproic acid or tranexamic acid may be used in some instances
- DDAVP may be useful in von Willebrand disease and platelet function disorders
Iliopsoas Bleeding

- Patient may complain of hip or groin pain
- Pain with extension and internal rotation
- In severe cases may have femoral neuropathy
- Patient typically adopts a hip-flexed position
- Usually requires extended treatment to resolve

Hematuria

- Vigorous oral hydration
- Bedrest
- May consider prednisone or specific hemostatic therapy for persistent bleeding
- Generally avoid aminocaproic acid

Surgery

- All patients getting elective surgery should have a treatment plan specified preoperatively
- For urgent surgery, attempt to achieve normal hemostasis
  - 100% correction preoperatively for hemophilia patients
- Follow-up therapy depends on the nature of the surgery
Sports and Bleeding Disorders

- Activity restrictions should be minimized
- No collision sports (football, hockey, lacrosse, boxing, rugby)
- No wrestling if they have hemophilia
- Most other sports participation OK if it doesn’t produce excessive bleeding
- Bike helmets and appropriate protective equipment should be used

The Primary Care Provider and Bleeding Disorders

- Primary care providers can help facilitate timely community-based emergent treatment
- Interface with school and community
- Primary care providers should be aware of what patients should be screened for bleeding disorders
- All patients with bleeding disorders need general pediatric care including health supervision with anticipatory guidance and appropriate health screening

The Nurse and The Bleeding Disorder Patient

- Education – point patients/families to appropriate current resources
- Practical Care – help patients/families deal with day-to-day issues surrounding bleeding disorders
- Reassurance – having a child diagnosed with a bleeding disorder can be very anxiety provoking, even though most patients will be fine