Management of Pediatric Hematologic Emergencies

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• None
Objectives

• Diagnosis
• Management
  Hem-Onc emergencies
• Bleeding (thrombocytopenia)
• Anemia
Hematology - Oncologic Emergencies

- Metabolic/endocrine as a result malignancy or therapy
- Lesions press/obstruct vital organs
- Pancytopenia secondary to malignancy or chemotherapy-hemorrhage/anemia/infection
- Organ dysfunction/failure
Other Hematologic Emergencies

• Thrombosis (previous lecture)
• Bleeding
  Thrombocytopenia
• Anemia
Oncologic emergencies
Hyperleukocytosis

- WBC > 100,000/mm$^3$
- Increased blood viscosity/tumor emboli microcirculation
- Intracranial hemorrhage, thrombosis, pulmonary hemorrhage, leukostasis
- Tumor lysis
- 23% mortality ANLL and 5% ALL
Fig. 1. Therapeutic approach to acute hyperleukocytosis. TLS tumor lysis syndrome, TLC total leukocyte count, AML acute myeloid leukemia, ALL acute lymphoblastic leukemia, APL acute promyelocytic leukemia, RBC red blood cell, Hb hemoglobin, PLTs platelets, CHF congestive heart failure.
Tumor lysis

• Occurs bulky B cell or T cell leukemias or lymphomas

• Rapid lysis or cell death leading to hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia

• If not treated: cardiac arrhythmias, renal failure, seizures, coma, DIC, death
TLS: Risk stratification and treatment

- **Low risk**
  - Uric acid <7.5
  - Indolent NHL

  Hydration/close monitoring

- **Intermediate**
  - Uric <7.5
  - LDH
  - Bulky disease (>10 cm)

  Aggressive hydration/rasbicurase if uric acid rises despite allopurinol

- **High risk**
Burkitt’s Lymphoma
Management tumor lysis

- Monitor I/O, sp gravity, pH
- Monitor lytes, Ca, PO4, uric acid q 6 hrs
- Cardiac monitoring if hyperkalemia or hypocalcemia
- Hydration, allopurinol, rasburicase
Figure 2 Algorithm for the management of tumor lysis syndrome (TLS) [3,13,34]. CMP, complete metabolic panel; EKG, electrocardiogram; G6PD, glucose-6-phosphate dehydrogenase; IV, intravenous; LDH, lactic dehydrogenase; PO, by mouth.
Thoracic Emergencies

- **SVC syndrome**

  - **Etiology:** thrombosis, malignant anterior mediastinal masses (Hodgkin’s, NHL, teratoma or other germ cell tumors)

  - **Signs and symptoms:** swelling, plethora, cyanosis face, neck and upper extremity

- **SMS**

  - cough, hoarseness, dyspnea, orthopnea, chest pain
SVC syndrome

Management

• Prevent: supine position, stress, sedation
• Might need intubation (extubation until decrease size mass)
• ECMO
• Dx: CXR or CT, needle biopsy, serum markers
• Tx: thrombosis-thrombolytics if clot, malignancy (rad tx, steroids -pred 40 mg/m2, chemotherapy)
Infection

• Comprehensive evaluation of the patient (vital signs, complete exam including perfusion)
• Gram positive and gram negative coverage
• Consider anaerobic coverage [if abdominal pain, perirectal findings (fissure, redness, pain)].
• Fluid resuscitation/blood transfusion if needed
• Continue antibiotics until count recovery (rising absolute neutrophil count, neg blood cx, no fever)
• Antifungal therapy
Typhylitis

- Necrotizing colitis localized cecum
- Severe neutropenia
- Right lower quadrant pain
- Clostridium and Pseudomonas
- Mortality 50-100%
- Dx: clinical and CT
- Management: antibiotics, bowel rest if severe

www.emedicine.com/ardio/images
Perirectal abscess

- Perirectal pain, tenderness, painful bowel movements
- Antibiotics to cover gram neg and anaerobes
- GCSF/granulocyte transfusions
- Surgical (debridement, colostomy)
Neurologic Complications

- Spinal cord compression: 3-5% children with cancer
  - Sarcomas account ½ (remainder lymphoma, neuroblastoma, leukemia)
  - Metastases (brain tumors)
- Back pain
- Incontinence, urinary retention
- Loss strength and sensory deficits
Spinal cord compression

- Dexamethasone 1-2 mg/kg loading dose (max 10 mg) followed by 1.5 mg/kg/day (max 4 mg/dose)
- Mild deficits (0.25-1 mg/kg q 6 hrs)
- Epidural mass (decompression-surgical, chemotherapy, radiation)
Seizures

• Stabilize patient
• Evaluate CT/MRI
• Etiologies (brain tumor, sinus-venous CNS thrombosis, bleeding, PRES)
• Tx: treat underlying disorder
Evaluation Bleeding Disorders
Bleeding assessment

Bleeding history

Age/gender

Location:

Skin/mucous membranes: plt and blood vessels
Soft tissue/muscles/joints: coagulation factor

Medications

Other abnormal bleeding: circumcision, dental extraction, menses, surgery?

Abnormal bruising or bleeding

- Frenulum bleeding (more severe if hemostatic disorder)
- Retinal (uncommon), Fractures (uncommon) non-accidental trauma?
- ICH (outside neonatal period)
- Umbilical cord bleeding or delayed separation?
- Prolonged bleeding heelprick?
- Hematoma formation (vit K, immunizations?)
# Clinical Evaluation

<table>
<thead>
<tr>
<th>Bleeding Characteristics</th>
<th>Platelet Disorders</th>
<th>Plasma coagulation disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Superficial, Mucosal</td>
<td>Deep</td>
</tr>
<tr>
<td>Types</td>
<td>Petechiae, Purpura</td>
<td>Hematomas/ecchymoses</td>
</tr>
<tr>
<td>Size</td>
<td>Smaller</td>
<td>Larger</td>
</tr>
<tr>
<td>Timing</td>
<td>Immediate, mild</td>
<td>Delayed, severe</td>
</tr>
<tr>
<td>Example</td>
<td>Menorrhagia, Epistaxis, palatal petechiae</td>
<td>Hemarthroses, soft tissue hematomas</td>
</tr>
</tbody>
</table>
Clinical Evaluation

PHYSICAL EXAMINATION

- Skin and Mucosa
  - Petechiae (1-2mm), Purpura
  - Ecchymoses (>10mm)
  - red/purple, non-blanching subcutaneous hemorrhage
Clinical Evaluation

PHYSICAL EXAMINATION

▪ Skin and Mucosa
  ▪ Telangiectasias
    - permanent dilation of superficial blood vessels
  ▪ Hemangioma
    - typically benign tumor of blood vessels
Clinical Evaluation

PHYSICAL EXAMINATION

▪ Musculoskeletal system
  ▪ Hemarthroses, Hypermobility, skin hyperextensibility
Clinical Evaluation

PHYSICAL EXAMINATION

• Skin and Mucosa
  • Bruising patterns
Bruising Areas

Normal Bruising Areas
- Elbows
- Knees
- Shin

Suspicious Bruising Areas
- Back
- Back of Thighs
- Back of Calves
- Buttocks

https://www.abusewatch.net/child_medimage.php
Clinical Evaluation

- Red flag abuse
  - unusual location
  - inconsistent with the injury
  - no explanation offered for the injury
  - inconsistent with the child's developmental level
  - blamed on another child or sibling
  - multiple bruises at various stages of healing

- Documentation is key
  - Objective, complete
    - Location, size, color, description
    - Document with medical pictures – Extremely important
Investigation hemostatic system in children with bruising or bleeding

- CBC and peripheral smear
- PT, aPTT
- Fibrinogen
- TT
- Factor XIII screen
- vWD (factor VIII, von Willebrand antigen, RCo activity)
- Platelet function
# Classification

<table>
<thead>
<tr>
<th>Inherited</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia A and B</td>
<td>Vitamin K deficiency</td>
</tr>
<tr>
<td>von Willebrand Disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Deficiency factors II, V, VII, X, XI, or XIII</td>
<td>DIC</td>
</tr>
<tr>
<td>Dys-, hypo- or afibrinogenemia</td>
<td>Massive transfusion</td>
</tr>
<tr>
<td>alpha-2 antiplasmin</td>
<td>Malignancy</td>
</tr>
<tr>
<td>PAI-1 deficiency</td>
<td>Coagulation inhibitors</td>
</tr>
<tr>
<td>Platelet (dysfunction, production)</td>
<td></td>
</tr>
<tr>
<td>Munchausen</td>
<td></td>
</tr>
<tr>
<td>Spurious lab tests</td>
<td></td>
</tr>
</tbody>
</table>
Treatment

- Factor replacement (Factor VIII/IX deficiency)
- Antifibrinolytics (Tranexamic acid, Aminocaproic acid)
- DDAVP
- Cryoprecipitate, Fibrinogen concentrate (RiasTap)
- Recombinant Factor VII
- Hormonal therapy (menorrhagia)
- FFP
- Platelets
Disseminated Intravascular Coagulation

- DIC: systemic activation of blood coagulation, generation intravascular thrombin and fibrin.

- Three types:
  1. Bleeding: hyperfibrinolysis predominant (e.g. leukemias)
  2. Organ failure type: hypercoagulation (e.g. sepsis)
  3. Major bleeding: hypercoagulation and hyperfibrinolysis (e.g. surgery)
DIC

- Infection
- Malignancy
- Vascular malformation (e.g. hemangioma)
Acute Promyelocytic Leukemia
General guidelines

• Administration red blood cells and platelets patients bleeding or at risk bleeding

• FFP 15 ml/kg (if concerns fluid overload, consider prothrombin concentrates)

• Low fibrinogen: cryoprecipitate or fibrinogen concentrates

• Heparin: only thrombosis predominant DIC
Platelet Disorders

- Thrombocytopenia
  - Platelet count of less than 150,000/microL
Causes of thrombocytopenia

<table>
<thead>
<tr>
<th>Table 1. Causes of Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Increased Platelet Destruction</strong></td>
</tr>
<tr>
<td>• Immune-mediated</td>
</tr>
<tr>
<td>- Immune thrombocytopenic purpura</td>
</tr>
<tr>
<td>- Neonatal alloimmune thrombocytopenia</td>
</tr>
<tr>
<td>- Neonatal autoimmune thrombocytopenia</td>
</tr>
<tr>
<td>- Autoimmune diseases</td>
</tr>
<tr>
<td>- Drug-induced</td>
</tr>
<tr>
<td>• Platelet activation/consumption</td>
</tr>
<tr>
<td>- Disseminated intravascular coagulation</td>
</tr>
<tr>
<td>- Hemolytic-uremic syndrome</td>
</tr>
<tr>
<td>- Thrombotic thrombocytopenic purpura</td>
</tr>
<tr>
<td>- Kasabach–Merritt syndrome</td>
</tr>
<tr>
<td>- Necrotizing enterocolitis</td>
</tr>
<tr>
<td>- Thrombosis</td>
</tr>
<tr>
<td>• Mechanical platelet destruction</td>
</tr>
<tr>
<td>• Platelet sequestration</td>
</tr>
<tr>
<td>- Chronic liver disease</td>
</tr>
<tr>
<td>- Type 2B and platelet–type von Willebrand disease</td>
</tr>
<tr>
<td>- Malaria</td>
</tr>
<tr>
<td><strong>Decreased Platelet Production</strong></td>
</tr>
<tr>
<td>• Infection</td>
</tr>
<tr>
<td>• Cyanotic congenital heart disease</td>
</tr>
<tr>
<td>• Bone marrow failure or infiltrate</td>
</tr>
<tr>
<td>- Acute lymphoblastic leukemia and other malignancies</td>
</tr>
<tr>
<td>- Acquired aplastic anemia</td>
</tr>
<tr>
<td>- Fanconi panmyelopenia</td>
</tr>
<tr>
<td>• Nutritional deficiencies</td>
</tr>
<tr>
<td>• Genetically impaired thrombopoiesis</td>
</tr>
<tr>
<td>- Thrombocytopenia with absent radii syndrome</td>
</tr>
<tr>
<td>- Congenital amegakaryocytic thrombocytopenia</td>
</tr>
<tr>
<td>- Wiskott–Aldrich syndrome</td>
</tr>
<tr>
<td>- X-linked thrombocytopenia with thalassemia</td>
</tr>
<tr>
<td>- Giant platelet disorders</td>
</tr>
<tr>
<td>- Bernard–Soulier syndrome</td>
</tr>
<tr>
<td>- May–Hegglin/Fechtner/Epstein and Sebastian syndromes</td>
</tr>
</tbody>
</table>

[Thrombocytopenia in Infants and Children](#)

Deborah M. Consolini

*Pediatrics in Review* 2011;32:135

DOI: 10.1542/pir.32-4-135
Figure 2. Diagnostic algorithm for thrombocytopenia. CAMT = congenital amegakaryocytic thrombocytopenia, DIC = disseminated intravascular coagulation, HUS = hemolytic-uremic syndrome, TAR = thrombocytopenia with absent radii syndrome, TTP = thrombotic thrombocytopenic purpura, WAS = Wiskott-Aldrich syndrome.

Thrombocytopenia in Infants and Children
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Physical findings
<table>
<thead>
<tr>
<th>Table 4. Red Flags Suggesting a Diagnosis Other Than Immune Thrombocytopenic Purpura</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
</tr>
<tr>
<td>• Fever</td>
</tr>
<tr>
<td>• Bone pain</td>
</tr>
<tr>
<td>• Weight loss</td>
</tr>
<tr>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Recent history of infections or vaccinations</td>
</tr>
<tr>
<td>• Past medical history of diseases associated with thrombocytopenia (e.g., autoimmune disorders, cirrhosis)</td>
</tr>
<tr>
<td>• Dietary history suggestive of iron, vitamin B12, or folate deficiency</td>
</tr>
<tr>
<td>• Exposure to medications known to be associated with thrombocytopenia</td>
</tr>
<tr>
<td>• Travel history to an endemic area for malaria</td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
</tr>
<tr>
<td>• Lymphadenopathy</td>
</tr>
<tr>
<td>• Splenomegaly</td>
</tr>
<tr>
<td>• Joint swelling</td>
</tr>
<tr>
<td>• Short stature</td>
</tr>
<tr>
<td>• Limb defects, including radial agenesis and thumb abnormalities</td>
</tr>
<tr>
<td>• Cataracts</td>
</tr>
<tr>
<td>• Sensorineural hearing loss</td>
</tr>
<tr>
<td>• Oral leukoplakia</td>
</tr>
<tr>
<td>• Dystrophic nails</td>
</tr>
<tr>
<td>• Eczema in male patient</td>
</tr>
<tr>
<td>• Frequent infections</td>
</tr>
<tr>
<td>• Superficial hemangiomas</td>
</tr>
</tbody>
</table>
Summary

✅ History and physical exam are the best screening tests for bleeding disorders

✅ The absence of a family history of bleeding disorders does not exclude the diagnosis of a genetic disorder

✅ Thorough evaluation and documentation of bleeding symptoms are essential for identifying cases of non-accidental trauma

✅ Use pediatric reference values to assess laboratory findings based on a patient’s age

✅ Refer to a specialist if concerned about bleeding disorder
Anemia
Anemia

• Morphologic classification
  RBC indices (MCV)
  Hemoglobin content (MCH)

• Physiologic classification
  Decreased Production
  Increased Destruction
  Blood loss
History

- **Age**
  - Newborn
    - Congenital RBC disorder, perinatal loss, immune
  - Age 3-6 months
    - Congenital, RBC aplasia
  - Age >6 months
    - More often acquired (e.g. nutrition, TEC)

- **Gender**
  - X linked disorders (G6PD)

- **Race/Ethnic origin**
  - Thalassemia, sickle, Hgb E, G6PD etc.

- **Neonatal history**
  - Neonatal jaundice? HS, G6PD, ABO incompatibility
Diet

• Pica
  • Suggestive of iron deficiency.

• What kind of Milk
  • Whole milk (Fe def. if too early)
  • Goat’s milk (deficient in Folate)

• Vegan
  • Can be B12 deficient
Drugs

- Oxidant induced hemolytic anemia e.g. G6PD

- Drug induced megaloblastic anemia e.g. purine and pyrimidine analogs (6 MP, 5 FU)

- Drug and chemical induced aplastic anemia e.g. Chloramphenicol, insecticides, etc
History of Blood Loss

• GI blood loss

• Menstrual blood loss in teenage girls

• CNS bleeding does not cause anemia outside the newborn period
Evaluation of Anemia

- Detailed history and physical examination
- Complete blood count
- Determination of the morphologic characteristics based on blood smear, MCV and RDW
- Bone marrow aspiration
- Additional tests for specific type of anemia
Blood Film

- Exam for red cell morphology
- Exam for basophilic stippling and red cell inclusions
- Exam of other cell lines
# Normal Values of Hemoglobin

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Hemoglobin (g/dL)</th>
<th>Hematocrit (%)</th>
<th>MCV (μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Lower Limit</td>
<td>Mean</td>
</tr>
<tr>
<td>0.5–1.9</td>
<td>12.5</td>
<td>11.0</td>
<td>37</td>
</tr>
<tr>
<td>2–4</td>
<td>12.5</td>
<td>11.0</td>
<td>38</td>
</tr>
<tr>
<td>5–7</td>
<td>13.0</td>
<td>11.5</td>
<td>39</td>
</tr>
<tr>
<td>8–11</td>
<td>13.5</td>
<td>12.0</td>
<td>40</td>
</tr>
<tr>
<td>12–14:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13.5</td>
<td>12.0</td>
<td>41</td>
</tr>
<tr>
<td>Male</td>
<td>14.0</td>
<td>12.5</td>
<td>43</td>
</tr>
<tr>
<td>15–17:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>14.0</td>
<td>12.0</td>
<td>41</td>
</tr>
<tr>
<td>Male</td>
<td>15.0</td>
<td>13.0</td>
<td>46</td>
</tr>
<tr>
<td>18–49:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>14.0</td>
<td>12.0</td>
<td>42</td>
</tr>
<tr>
<td>Male</td>
<td>16.0</td>
<td>14.0</td>
<td>47</td>
</tr>
</tbody>
</table>
Other tests...

- Mentzer index: MCV/RBC mass
- >13 iron deficiency
- <13 Beta thalassemia
- Hemoglobin electrophoresis: rule out hemoglobinopathy (alpha Thal trait needs gene sequencing)
- Coombs, creatinine, bilirubin, LDH, haptoglobin, osmotic fragility, TSH
Management

• Transfusion: if severe and symptomatic

• Consider diagnostic evaluations prior to transfusion

• If anemia not symptomatic, treat underlying problem (e.g. iron in iron def anemia; prednisone: autoimmune hemolytic anemia).