Hematology: When to Keep Them and When to Refer Them

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Speaker Introduction

• Dr. Paige Johnson is a pediatric nurse practitioner at Children’s Mercy Hospital in Kansas City, Mo., in Hematology/Oncology. She has been a nurse for 25 years and a nurse practitioner for nearly 20 years. She graduated with her bachelor’s in nursing from the University of Kansas and her master’s in nursing from the University of Texas-Houston. She also has a masters in public health from Johns Hopkins University focusing on international maternal/child health and a DNP from the University of Kansas School of Nursing in 2016. She is also an adjunct professor at the University of Missouri-Kansas City in the MSN/DNP program. She has been working in pediatric oncology for more than 15 years.

Disclosures

I have no disclosures

Learning Objectives

• Differentiate abnormal lymphadenopathy from infectious/viral lymphadenopathy in pediatric patients.
• Explain causes of ITP and appropriate monitoring that can be done in the primary care setting.
• Analyze hematology labs and interpret abnormals through pediatric cases

Hematology Primer

Blood Cell Lines

National Cancer Institute, 2009
WBCs

- Protects the body from invasion by organisms and other immune system responses
- Normal count 5,000-10,000
- Elevated means infection or bone marrow dysfunction (leukemia)
- Low could be infection, autoimmune process, but also could be an oncologic disease

Cells in Differential

- Granulocytes
  - Cells have large granules in it
  - Horse-shoe shaped nuclei connected by thin strands
  - Cytoplasm stains blue
  - Neutrophils, basophils, eosinophils
- Agranulocytes
  - Lymphocytes, monocytes

Granulocytes

- Neutrophils (also PMNs or Polys)
  - 40-70% of differential
- Basophils
  - Less than 1% of circulating cells
- Eosinophils
  - 1-2% of WBCs

Agranulocytes

- Lymphocytes
  - 25-35% of WBCs
- Monocytes
  - 4-6% of WBCs

Hemoglobin

- Normals
  - 2wks: 13-20
  - 3mo: 9.5-14.5
  - 6mo-6ys: 10.5-14
  - 7-12yrs: 11-16
  - Menstruating females: 13-16
  - Teen/adult males: 14-18
  - Decreased with RBC destruction, chemotherapy, anemia, bleeding
  - Increased with polycythemia, high altitudes, chronic lung disease

Reticulocytes

- Young RBCs
  - After release from bone marrow
  - Stay in circulation for 1 day before maturing to RBCs
  - Reticulocyte count
  - % of circulating RBCs
  - Reflect bone marrow production of new RBCs
  - Will be low in anemia
Other Values with Hemoglobin

- Hematocrit: % of RBCs in a given volume of blood (deciliter)
- RBC count: how many circulating RBCs
  - High with volume loss, diarrhea, burns, dehydration, polycythemia
  - Low with anemia
- Mean corpuscular volume (MCV): volume of the average RBC
  - High (macro) with B12 (folate) deficiency or hypothyroid
  - Low (micro) with Fe deficiency, thalassemia, Pb poisoning, anemia of chronic disease
- Mean corpuscular Hgb (MCH): amount of Hgb in the RBC—mirrors MCV

Other Values with RBCs

- Ferritin
  - Increased with iron overload (repeated transfusions), ESRD, spherocytosis, megaloblastic anemia, porphyria
  - Decreased with iron def
- Total Iron Binding Capacity (TIBC)
  - Increased with iron def, acute/chronic blood loss, acute liver damage
  - Decreased in hemochromatosis, cirrhosis, thalassemia, nephrosis, hyperthyroidism, chronic infection
- Serum Iron
  - Increased in excessive iron intake (iron therapy, transfusions), decreased RBC formation, acute liver damage, pregnancy, hemochromatosis
  - Decreased in iron def, neoplasms, nephrosis, menstruation

Platelets

- Normal is 150,000 to 300,000
- Smallest cellular component
- Fragments of megakaryocytes (precursor in BM)
- When bleeding occurs
  - Platelets go to site, form hemostatic plug
  - As degrade, cause release of clotting factors
- Bring about clotting cascade
  - Increased with sudden exercise, trauma, fracture, after surgery, leukemia, after childbirth, Fe def
  - Decreased with DIC, ITP, HUS, burns, marrow suppression, viral infections, ASA use, pre/eclampsia

Common Primary Care Issues

Lymphadenopathy

What is it?

- Term that indicates any abnormality of a lymph node
  - Lymphadenitis indicates inflammation of a lymph node
  - Can be regional or systemic
    - If regional, nodes that are proximal to the infection will be enlarged
  - Can be acute or chronic
    - Acute are usually tender to the touch
    - Chronic may be non-tender
What to think about

- Common Infection causes:
  - Bacterial
  - Viral (EBV, CMV, HIV)
  - Parasitic (toxoplasmosis)
  - STDs (Syphilis)

- Rare Causes:
  - Leukemia, Lymphoproliferative diseases, LCH, Lymphoma
  - TB
  - Measles
  - SLE/RA
  - Sarcoidosis
  - Fungal infections, plague
  - Drug reactions

What is Normal?

- Most lymph nodes are not palpable in newborns
- Cervical, axillary, inguinal nodes can sometimes be palpable in children
- Posterior cervical nodes with URIs, allergies
- It is not considered abnormal until the diameter exceeds 1cm for cervical and axillary; 1.5 cm in inguinal
- Generalized adenopathy is not normal and systemic illness should be suspected
- Firm, fixed nodes should be suspicious for cancer
- Usually nontender, rubbery in consistency

Work up

- Should be considered infectious until otherwise proven
- Detailed history and physical
- Diagnostics-labs, micro studies (EBV, CMV, HIV, Bartonella), TB; CT or US if needed, biopsy is last resort
- If infection, should respond to treatment. Failure to respond after 14 days, requires more work up.

When to Refer to Hematology

- Lymph nodes that don’t respond to therapy
- Abnormal CBC
- Other symptoms-weight loss, night sweats, fevers
- Supraclavicular lymph nodes

What is it?

- A decrease in the absolute number of circulating neutrophils (segs and bands) in the peripheral blood
  - Absolute Neutrophil Count (ANC)=Bands + Segs X Total WBC count/100 (in %)
  - Low normal is 1500 in children under 12mo
  - Can be acute or chronic

Neutropenia
### What is it?

- **Acquired Disorder**
  - Aplastic Anemia
  - Vit B12, copper, folate deficiencies
  - Leukemia (ALL, AML)
  - Myelodysplasia
  - Prematurity with birthweight <2kg
  - Paroxysmal nocturnal hemoglobinuria (stem cell defect)

- **Extrinsic Insult**
  - Infection (such as Flu A/B, HHV6, RSV, Enterovirus, Parvo B19, EBV, CMV, HIV, severe bacterial inf, rickettsial or fungal inf)
  - Drug induced (suicide, PCN, antipsychotics, antithyroid, anti‐rheumatologics, antipyretics)
  - Immune neutropenia (autoimmune)
  - Reticuloendothelial sequestration (hypersplenism)
  - Bone marrow replacement (myelofibrosis, malignancy)
  - Chemotherapy/radiation

### Neutropenia of Infancy

- **Autoimmune neutropenia (AIN) of infancy:**
  - AIN in older children can be related to other conditions (autoimmune disorders, complications of infection, drugs, malignancy)
  - Treat underlying disorder

- **Neonatal passive autoimmune neutropenia**

### Presentation

- Those with ANC less than 500, are at high risk for infections
- Fever, stomatitis and gingivitis are most common presentation
- Also can present with whole host of infections
- Most common pathogen is *Staphylococcus aureus* and gr- bacteria
- Typical presentation of infections (exudate, fluctuance, LAD) may be diminished due to neutropenia

### Other Neutropenias

- **Cyclic Neutropenia:**
  - Autosomal dominant congenital granulopoietic disorder
  - Rare: 0.5-1 case per 1 million
  - Oscillatory period of about 21 days; ANC can be normal to <200
  - Need to get serial labs 3 times a week for 6-8 weeks to diagnose

### Treatment

- Treat underlying process, if exists
- Remove offending drug
- G-CSF can be helpful in those with serious neutropenia to reduce risk of severe infection
- Refer to hematology for guidance
**Immune Thrombocytopenic Purpura (ITP)**

**What is it?**
- Most common cause of thrombocytopenia in well children
- Usually occurs 1-4 weeks after a viral infection
- Autoantibody develops against platelet surface antigen
- Sudden onset of thrombocytopenia
- No difference between males and females
- Seems to have a seasonal prevalence - late Winter and early Spring are times of higher respiratory viral illnesses
- Most common viruses have been associated with it including EBV and HIV
- Approximately 20% of children develop chronic ITP (longer than 90 days)

**Diagnosis**
- Thrombocytopenia, platelet count less than 20,000
- WBC, Hgb, differential should be normal
- Bone marrow evaluation not necessary unless have abnormal CBC results

**Clinical Presentation**
- Sudden onset of generalized petechiae and purpura
- May be bleeding from gums and mucous membranes
- PE is usually normal apart from petechiae and purpura
- Splenomegaly, lymphadenopathy, bone pain and pallor are rare.

**Treatment (2019 ASH Guidelines)**
- Refer to Hematology
- For Children with platelet count <20,000 who have no or mild bleeding (skin manifestations only - bruising or petechiae)
  - Observation is recommended
  - Children with mucocutaneous bleeding/Non-life threatening mucosal bleeding (Refer to Hematology)
  - Corticosteroids: Prednisone-1.4mg/kg/24hours for 7 days until platelet count rises above 20,000
  - Immunglobulin (IVIG)-0.8-1gm/kg/day for 1-2 days
- Nplate vs Rituximab for ITP that doesn't respond to first line therapy

**Iron Deficiency Anemia**
What is it?
- Iron deficiency is a world-wide problem
- Significantly can increase the risk of developmental delays and behavioral issues
- Most common causes are LBW, prematurity, exposure to lead, exclusive breast feeding beyond 4mo, weaning of whole milk to non-iron fortified formula
- Other factors: feeding problems, poor growth, low SES, children with special health care needs

Iron Requirements (AAP/WHO)
- Iron requirements differ with age:
  - Pre-term: 2mg/kg/day by 1mo of age through 12mo of age
  - Term Breastfed: add 1mg/kg/day starting at 4mo if exclusively breastfed
  - Term, Formula-Fed: iron fortified formula is 12mg/L is standard
  - Toddlers (1-3 yrs): 7mg/day through foods or supplementation if a picky eater

Symptoms of IDA
- Usually asymptomatic
- Lethargy/decreased energy
- Pale
- Poor Feeding
- Tachypnea
- PICA-craving of nonfood items (ice, paper, dirt, rocks, chalk, soap)

Diagnosis
- Low hemoglobin for age and elevated MCV

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<th>Average Normal High</th>
<th>Diagnostic of High</th>
<th>MCV</th>
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<tr>
<td>5-12 years</td>
<td>13.5</td>
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Dietary Considerations
- Infants younger than 12mo:
  - Breast fed or receive iron-fortified formula.
  - If exclusively breastfed at 4mo, add iron supplement
  - Cow’s milk can cause cow’s milk protein induced colitis leading to intestinal blood loss
- Children over 12mo:
  - Cow’s milk should be limited to 24 oz (AAP, 2019)
  - Introduce other sources of dairy
  - Introduction of iron rich foods (~3 servings a day is ideal)
References


Resources