“Does Morphology Matter in 2017”

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ISLH
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Objectives

• Recognize unique RBC and WBC abnormalities in non-neoplastic disorders

• Learn key strategies for differential diagnosis assessment in blood and bone marrow

• Appreciate integrative nature of non-neoplastic case workup
Outline

• Peripheral blood clues to non-neoplastic RBC and WBC disorders
• Key BM tip offs for selected non-neoplastic disorders
RBC Disorders

• Essential CBC data regarding number, size, shape, uniformity, hemoglobin content, reticulocyte count

• Morphologic assessment for key RBC abnormalities:

  1. Inclusions
  2. Fragmentation
  3. Unique shapes; oval macrocytes
  4. Erythrophagocytosis
Microangiopathic Hemolytic Anemia Picture

- Spherocytes, schistocytes present in setting of anemia
- Markedly increased RDW (>30%)
- Macrocytosis
- Other CBC findings: Thrombocytopenia
- Patient may have neurologic symptoms
Case 1

42-yr-old male with 2 week history SOB, gum bleeding, tingling sensation in upper and lower extremities, weight loss, malaise, weakness.
# Case 1

<table>
<thead>
<tr>
<th>CBC</th>
<th>WBC</th>
<th>3.2</th>
</tr>
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<tbody>
<tr>
<td>RBC</td>
<td>1.19</td>
<td></td>
</tr>
<tr>
<td>Hgb</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>Hct</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>MCV</td>
<td>122</td>
<td></td>
</tr>
<tr>
<td>RDW</td>
<td>30.7%</td>
<td></td>
</tr>
<tr>
<td>Plt</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Retic</td>
<td>5.9%</td>
<td></td>
</tr>
<tr>
<td>4 NRBC/100WBC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Blood-Pancytopenia
Blood-Pancytopenia
Differential Diagnosis:

1. TTP (clinical diagnosis)
2. HUS
3. Megaloblastic anemia
4. MDS
5. Other(?)

What additional information needed?
Additional Labs

Absolute retic 0.07 NL

Haptoglobin < 8 ↓

LDH 1600 ↑

Vitamin B_{12} 93 ↓
Case 1: Diagnosis

• Megaloblastic anemia mimicking TTP

Reference:
Follow Up Labs

ADAMTS13: 71 mL
MMA: 3.08 ↑
IF ab: positive
Shiga toxin: negative

Reference:
Case 1: Key Tips

• Meg anemia can manifest with pancytopenia

• Oral macrocytes broken in spleen (schistocytes, ↑ RDW)

• MCV 122 — not due to reticulocytes

• Retic % was elevated but not absolute retic count
Key Tips

• MCV >120
• Hypersegmentation
• Megaloblastic changes in NRBC’s (search at feather)
• Neurologic symptoms typical in megaloblastic anemia
Case 2

• Hemophagocytosis in blood
Neutrophil, monocyte
Severe anemia
Severe anemia, monocyte
What information is needed?

- Age
- Recent medical history
- Serologic tests
Erythrophagocytosis: Key Tips

**Blood:** Often immune-mediated
RBC’s only

**BM:** Many causes
Nonspecific when minimal and just RBC’s ingested
HLH: many histiocytes with ingested RBC’s and other HP cells
Case 2: Diagnosis

- Paroxysmal cold hemoglobinuria (PCH)
- Child with prolonged cold exposure who presented to ER with profound anemia, cardiac failure, died in ER
Hemophagocytic Lymphohistiocytosis (HLH)

Primary: Underlying immunodeficiency
Perforin mutations common
Repeated episodes of HLH, often triggered by EBV infection

Secondary: Triggered by infection (usually EBV) in setting of acquired/iatrogenic immunodeficiency (e.g. post SCT)

Neoplasm-associated: T-cell neoplasms (e.g. subcutaneous panniculitis-like T-cell lymphoma)
May occur in setting of BM involvement by neoplasm OR BM negative for neoplasm

HLH: Diagnostic Criteria: (5 of 8 Required)

1. Fever
2. Splenomegaly
3. Bicytopenia
4. Hypertriglyceridemia/hypofibrinogenemia
5. Hemophagocytosis
6. Low/absent NK activity
7. Hyperferritinemia
8. High soluble IL-2- receptor levels
Erythrophagocytosis
(vs hemophagocytosis)

**Blood:** Uncommon usually just RBC’s ingested

**BM:**
1) Fairly common especially in febrile, severely ill patients
2) Rare hemophagocytic histocytes-non-specific
3) Frequent hemophagocytic histiocytes clue to HLH
Lymphocytes in Blood

- Clinical features: Age is key!, splenomegaly, lymphadenopathy
- Absolute lymphocyte count-age related variations in normal range
- Other CBC information (status of hematopoietic cell production)
Lymphocyte Morphology in Blood

• Activated vs non-activated
• Blastic vs mature-appearing
• Round vs irregular nuclei
• Distinctive features
  a. Cytoplasmic granules
  b. Cytoplasmic vacuoles
  c. Irregular cell membrane borders
Case 3

• 3 month old boy with acute GI symptoms

  WBC  38.4
  H/H  11.4/35
  Plt   256
  ANC  26.0
  ALC  11.0
Non-Activated Lymphocytes

Vacuolated lymphocytes
Non-Activated Lymphocytes

Vacuolated lymphocytes
Differential dx:

• Normal for age

• Pathologic:
  Non-neoplastic vs Neoplastic
Case 3: Diagnosis

- Gangliocytosis type I (positive family history; positive genetic testing)

Other LSD: Sialic acid storage disease
Lymphs in Young Child: Distinct Vacuoles/Granules

Lysosomal storage disease (several types)
Vacuolated Lymphocytes in Adult

• Discrete vacuoles
• Clue to neoplasm
• Assess morphology
• Consider flow cytometry
Discrete vacuoles in lymphocytes as a subtle clue to mantle cell lymphoma

Ref: Lynch DT, Foucar K. Blood 2016; 127: 3292
Non-Activated Lymphocytes

Predominance of CD4+ T cells
Non-Activated Lymphocytes

Predominance of CD4+ T cells
Diagnosis:

Child: Pertussis

Adult: Likely T cell leukemia
Activated Lymphocytes

Infectious mononucleosis
Case 4

• 10-month-old male with a history of bowel resection for Hirschsprung’s disease. Patient on TPN; recent sepsis
Case 4

WBC  5.2
RBC  3.2
Hgb  7.1
Hct  22%
MCV  67
Plt  444
Medical Technologist Referral

10-month-old male
Medical Technologist Referral

Blood: 10-month-old male
Case 4: Key Features

CBC: Anemia, neutropenia

Key blood features: Hypochromic, microcytic anemia, Immature lymphocytes

Blood dx: Nutritional anemia, Lymphocytes physiologic for age

BM, flow: Not done
Case 4: Diagnosis

• Lymphocyte morphology within normal range for age
• Cytopenias explained by other findings
Morphology Key

• Assessment of RBC’s, neutrophils, monocytes and lymphocytes (platelets, too)

• Integration with CBC/other lab data and clinical information essential
Distinctive Findings are clue to Diagnosis

- **RBC**: Wide spectrum of blood findings in megaloblastic anemia
- **Hemophagocytosis**: Likely immune-mediated in blood
- **Lymphocytes**: Many distinctive morphologic features linked to non-neoplastic disorders