Evaluating the Abnormal CBC

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Learning Objectives

• How do I evaluate a patient with anemia or polycythemia?
• What are the common possibilities of low or high WBCs?
• How should I approach a patient with lymphocytosis?
• What is the most efficient evaluation of a patient whose platelets are too low, or too high?
ANEMIA

- Normocytic Normochromic
  - Reticulocyte Low/Normal
    - Renal insufficiency or failure
    - Bone marrow infiltration by cancer cells
    - Anemia of chronic disease
    - MDS
    - Combined anemia
    - Others
  - Reticulocyte Increased
    - Acute hemorrhage
    - Hemolytic anemia
    - Combined anemia
    - Others
  - Ferritin Low
    - Iron deficiency anemia
  - Ferritin NL/Increased
    - Thalassemia
    - Sideroblastic anemia
    - Anemia of chronic disease
    - Others

- Microcytic Hypochromic
- Macrocytic Hyperchromic
  - Reticulocyte Low/Normal
    - Prior hemorrhage
    - Prior hemolysis
    - Treated def. of Vit b12 / folate
    - Others
  - Reticulocyte Increased
  - Non-Megaloblastic
    - Liver disease
    - MDS
    - Hypothyroidism
    - Others
  - Megaloblastic
    - Vitamin B12 deficiency
    - Folate deficiency

Adapted with modifications from Wintrobe’s Clinical Hematology, 9th ed., 1993.
Patient 1

- 48 y/o F presents with fatigue and exertional dyspnea for 2 months
- Hgb 8.7
- MCV normal, MCHC 34, RDW 17.1 (nl<15.6)
- WBC 3.6 with normal differential
- Platelet count 498 (nl: 140-415)
- Lab data:
  - Stool guaiac: negative
  - Iron studies: iron 24, TIBC 411, iron saturation 9%, and ferritin 11
  - Vitamin B12 193 (nl>193), Folate mid normal
Are iron studies indicated with nl MCV?

- Not uncommon to see patients with documented iron deficiency to be replaced and MCV go from 80 to 93 (both normal) and RDW fall from 16 to 13
- Reticulocyte count will start rise in 2 weeks
- Iron studies help with suspicion of chronic disease: low iron, low TIBC, normal or low iron saturation and normal or high ferritin
- Discordance of ferritin and Fe/TIBC
- Treatment with iron replacement may not be effective
Management of patient 1

• Mixed deficiency of iron and vitamin B12, which presents with normocytic normochromic anemia

• Hypersegmented neutrophils suggest vitamin B12 deficiency

• Thrombocytosis could occur when iron deficient

• Leukopenia happens when vitamin B12 deficient

• Patient was treated with both iron and vitamin B12 supplements with partial improvement of her cell counts.
Lab work for patient 1 in two months

- Hgb 9.5
- MCV 78, MCH 23, MCHC 27
- WBC 4.5 and normal differential
- Platelet count 480 (nl: 140-415)
- Iron studies: iron 44, TIBC 411, iron saturation 17%, and ferritin 21
- Vitamin B12: 433; folate remains normal

IRON DEFICIENCY ANEMIA

- What we should do now?
Management of iron deficiency anemia not responding to oral iron

- Patient not taking oral iron (e.g., due to side effects)
- Reduced absorption of oral iron
- Blood loss exceeds iron intake
- Incorrect initial diagnosis
- More than one diagnosis (especially relevant in older adults)
- Inflammatory with block in intestinal iron regulation
- Therapy was effective but bleeding recurred

Management

- Could check auto abs:
  - anti-tissue transglutaminase (tTG) antibodies.
  - endomysial antibodies (EMA)
  - deamidated gliadin peptide (DGP) antibodies
- Patient was referred to GI for evaluation
- EGD with biopsy confirmed as celiac disease
- Patient received IV iron sucrose with Hgb improved to 11.8 now.
**ERYTHROCYTOSIS**

- Erythrocytosis with splenomegaly, thrombocytosis, leucocytosis
  - Polycythemia vera
    - \( \text{SaO}_2 > 92\% \)
      - Serum Epo
        - Serum Epo increased or high normal
          - P50
            - Decreased: 2,3 BPG deficiency, high affinity hgb methemoglobinemia
            - Normal: VHL mutation, epo-producing tumor
        - Serum Epo decreased or low normal
          - JAK2 mutation
            - Negative: PFCP
            - Positive: Polycythemia vera
  - Isolated erythrocytosis with no other abnormalities
    - \( \text{SaO}_2 < 92\% \)
      - Cardiac or pulmonary disease
Begin with the end in mind

- If the abnormalities are not only hemoglobin, but WBC and platelet counts, this will likely suggest a bone marrow problem. Referral is required.
- If the abnormality is only hemoglobin level, with normal MCV: the older the patient, the more likely this is a chronic disease
- Even younger patients could present with anemia of chronic illness/inflammatory anemia
  > Reticulocyte count, ESR, CRP, and SPEP, Cr, Epo level, LDH usually not helpful
White Blood cells

- Basophil
- Neutrophil
- Eosinophil
- Monocyte
- Small lymphocyte

Low or high

Peripheral smear review

Normal morphology
- Secondary causes
- Refer to hematology

Abnormal morphology
- Refer to hematology

No
## Look at Absolute Cell Count

<table>
<thead>
<tr>
<th>WBC (number/µl)</th>
<th>Normal</th>
<th>Case I</th>
<th>Case II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total WBC</td>
<td>4000-10000</td>
<td>4000</td>
<td>10000</td>
</tr>
<tr>
<td>% NEUTROPHILS</td>
<td>60%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>% lymphocytes</td>
<td>30%</td>
<td>80%</td>
<td>70%</td>
</tr>
<tr>
<td>Absolute neutrophils</td>
<td>4800</td>
<td>800</td>
<td>3000</td>
</tr>
<tr>
<td>Absolute lymphocytes</td>
<td>2400</td>
<td>3200</td>
<td>7000</td>
</tr>
</tbody>
</table>

Neutropenia But No Lymphocytosis  
No Neutropenia But Lymphocytosis
Patient 2 with lymphocytosis

- 70 y/o M presents for routine exam annually
- Absolute lymphocyte count 5.6, ANC 1.48
- Physical exam unremarkable
Consideration of Work Up

• Many neutrophilia or lymphocytosis of small degrees are transient and a repeat in 1-3 months is rational particularly post infection and post operation
• Fever? Adenopathy?
• Review of the peripheral blood smear!
• Polyclonal: EBV, CMV, VZV, hepatitis, HIV or splenomegaly?
• Peripheral protein markers
  Flow cytometry: monoclonal
  Typical B cell clones
    < 5k: monoclonal B lymphocytosis or SLL
    > 5k: CLL
  Non CLL
    B cell: mental cell, follicular, splenic marginal zone, hairy
    T cell: LGL (agranulocytosis), CTCL, T-CLL, prolymp
Characterize patient 2

- Lymphocyte count: 5.6
- Flow cytometry:
  - Expression CD5, CD19, CD20(dim), and CD23
  - Do not express CD10, CD38, CD103
  - B-cells: monocytic lambda
- Absolute B-cell count: 3.5
- Fish study negative for t(11;14)
- Diagnosis: Monoclonal B-cell lymphocytosis
Overview of Thrombocytopenia

- Significance of thrombocytopenia
  Current diagnosis of ITP: plt < 100k

- Platelet count nadirs

- Timing of onset of thrombocytopenia
Thrombocytopenia-Significance depends upon on its cause

- Post-cardiac / orthopedic surgery (~days 1-4)
  platelet = $60 \times 10^9$/L

- If HIT (~days 5-10)
  > High risk of venous and arterial thrombosis
  > Treat with non-heparin anticoagulant

- If sepsis (~days 2-3):
  > High risk of mortality (organ failure)

- If hemodilution (~days 0-1)
Median Platelet Counts: Q-ITP, TTP, HIT

Platelet count nadir (x10⁹/L), log scale

Warkentin T. Heamatol. ASH Educ Program 2016
Classification

- Pseudothrombocytopenia = spurious
- Hemodilution = fluids (esp. surgery)
- Consumption ~ physiologic: DIC, TMA
- Destruction = immune: auto-, allo-, drug
- Sequestration = hypersplenism (hypothermia)
- Decreased production = Pan>>isolated
Psuedothrombocytopenia
Classification

- Pseudothrombocytopenia
- Hemodilution
- Consumption
- Destruction
- Sequestration
- Decreased production

Postoperative thrombocytopenia
Postop Platelet Count Nadir

Orthopedic surgery data

Postop Platelet Count Nadir

Cardiac surgery data

Percent

Postoperative Day

Classification

- Pseudothrombocytopenia
- Hemodilution
- Consumption
- Destruction
- Sequestration
- Decreased production

Heparin induced thrombocytopenia
Classification

- Pseudothrombocytopenia
- Hemodilution
- Consumption
- Destruction
- Sequestration
- Decreased production

Cirrhosis (severe)
Platelet Count in Asians

<table>
<thead>
<tr>
<th>City</th>
<th>N</th>
<th>Mean ($\times 10^9$)</th>
<th>RI ($\times 10^9$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suzhou</td>
<td>274</td>
<td>119</td>
<td>60-259</td>
</tr>
<tr>
<td>Chengdu</td>
<td>218</td>
<td>120</td>
<td>52-202</td>
</tr>
<tr>
<td>Harbin</td>
<td>202</td>
<td>235</td>
<td>154-348</td>
</tr>
<tr>
<td>Kobe</td>
<td>294</td>
<td>239</td>
<td>151-346</td>
</tr>
</tbody>
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Thromb Haemost. 2002;88:111
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