Things to never miss in the office

Brett Houston MD FRCPC (PYG-5, hematology)
Leonard Minuk MD FRCPC
Presenter Disclosure

• Faculty / Speaker’s name: Brett Houston / Leonard Minuk

• Relationships with commercial interests:
  – Grants/Research Support: None
  – Speakers Bureau/Honoraria: None
  – Consulting Fees: None
  – Other: None
Learning Objectives

1. To review the red flags, diagnosis and approach to thrombotic thrombocytopenic purpura (TTP)

2. To review the common presentations of acute leukemia, and the immediate action plan
Learning Objectives

1. To review the red flags, diagnosis and approach to thrombotic thrombocytopenic purpura (TTP)

2. To review the common presentations of acute leukemia, and the immediate action plan
Case #1

- 44F with newly identified bruising / petechiae
- Vaginal bleeding since insertion of IUD one month prior; otherwise no bleeding

- Medical history: PCOS
- Medications: none
### Case #1

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10^9/L)</td>
<td>15</td>
</tr>
<tr>
<td>Differential (x10e9)</td>
<td>Neutrophils 11.9 Lymphocytes 2.73</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>68</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>98</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>330</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>11</td>
</tr>
</tbody>
</table>

- Creatinine 93
- ALT 10
- Total bilirubin 42
- Indirect bilirubin 33
- LDH 975
- Haptoglobin <0.01
Case #1

Peripheral film:
increased polychromasia;
4-10 schistocytes / hpf

Schistocytes
= Fragments
= Microangiopathy
Work-up of PANCYTOPENIA

RISK FACTORS / PRACTICE POINTS:

- Multiple Cytopenias
  - Blood Smear
    - Abnormal Cells Present?
      - NO
        - ANC < 1.5 x 10^9/L?
          - NO
            - Likely reactive / non-neoplastic due to drugs, critical illness, infections, connective tissue disease
            - Detailed History & Physical with particular attention to rule out ETOH / Cirrhosis
            - Referral to CCMB Hematology if persistent / symptomatic cytopenia
          - YES
            - Referral to CCMB Hematology for Suspected Home Malignancy, Dysplasia or AA
      - YES
        - If Blasts, NRBC, Dysplasia or Immature WBC
          - If Schistocytes
            - EMERGENT Referral to CCMB for Suspected TTP or IUS

- EMERGENT REFERRAL
  - Page Hematologist On-Call
  - Required for the following:
    - ANC < 0.5 x 10^9/L
    - Pt < 0 x 10^9/L
    - Symptomatic anemia in the absence of bleeding or iron deficiency (usually Hb < 70 g/L)
    - Blasts or schistocytes seen on the blood film

January 30, 2018: Hematology DGO in Review (Mitzman)
TTP – Clinical manifestations

• Classic pentad:
  – Fever
  – Thrombocytopenia
  – Microangiopathic hemolytic anemia
  – Neurologic symptoms
  – Renal insufficiency

Present in <10% of patients at diagnosis
TTP – Clinical manifestations

• *Thrombocytopenia (usually <30)
• *Thrombotic microangiopathy
• Neurologic symptoms (60%)
• Abdominal pain (mesenteric ischemia) (35%)
• Cardiac ischemia (25%)
• Renal failure (10-25%)
TTP - Investigations

- CBC
- Reticulocyte count
- Peripheral blood film
- Creatinine
- Bilirubin, LDH, haptoglobin
TTP – Differential diagnosis

• Malignant hypertension → Blood pressure
• Pre-eclampsia / HELLP → β-hcg
• Hemolytic uremic syndrome → Complement testing
• Disseminated intravascular coagulation → INR, aPTT, fibrinogen, d-dimer
TTP - Management

• Hematology referral (STAT → call)
• Plasma exchange

• Prior to plasma exchange, mortality in TTP was 90%
• With plasma exchange, survival in TTP is now 90%
Case #1 Revisited

• Despite feeling entirely well, 1 L of FFP was transfused and she sent to Winnipeg by ambulance
• Central line inserted in ER upon arrival
• Plasma exchange initiated within 4 hours
  – Hemoglobin, reticulocyte count, platelets and LDH normalized over the next few days
  – Currently under observation
Learning Objectives

1. To review the red flags, diagnosis and approach to thrombotic thrombocytopenic purpura (TTP)

2. To review the common presentations of acute leukemia, and the immediate action plan
Case #2

• 59F seen in clinic with increased bruising
• Otherwise well

• Past medical history: none
• Medications: none
# Case #2

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC (x10e9)</strong></td>
<td><strong>69</strong></td>
</tr>
</tbody>
</table>
| **Differential (x10e9)** | Neutrophils 0.7  
Lymphocytes 17.9  
Monocytes 1.4  
Myelocytes 0.69  
**Blasts 48.3** |
| **Hemoglobin (g/L)** | **109** |
| **MCV (fL)**     | **84** |
| **Platelets (x10e9)** | **27** |

* Prior CBC normal

* Atlas of Clinical Hematology, 6th Ed, 2004
## Case #2

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10e9)</td>
<td>69</td>
</tr>
<tr>
<td>Differential (x10e9)</td>
<td>Neutrophils 0.7</td>
</tr>
<tr>
<td></td>
<td>Lymphocytes 17.9</td>
</tr>
<tr>
<td></td>
<td>Monocytes 1.4</td>
</tr>
<tr>
<td></td>
<td>Myelocytes 0.69</td>
</tr>
<tr>
<td></td>
<td><strong>Blasts 48.3</strong></td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>109</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>84</td>
</tr>
<tr>
<td>Platelets (x10e9)</td>
<td>27</td>
</tr>
</tbody>
</table>

* Prior CBC normal

**IMPRESSION:**

- Leukocytosis (with blasts)
- Pancytopenia

Atlas of Clinical Hematology, 6th Ed, 2004
Case #3

• 24M seen in clinic with progressive fatigue, night sweats and weight loss
• Recently antibiotics for ?pneumonia
• No infectious source, no bleeding

• Past medical history: none
• Medications: none
Case #3

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10⁹/L)</td>
<td>1.9</td>
</tr>
<tr>
<td>Differential (x10⁹/L)</td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>1.19</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>0.71</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0.02</td>
</tr>
<tr>
<td>Blasts</td>
<td>0.02</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>97</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>94</td>
</tr>
<tr>
<td>Platelets (x10⁹/L)</td>
<td>153</td>
</tr>
</tbody>
</table>

* Prior CBC normal
Case #3

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC (x10⁹/L)</strong></td>
<td>1.9</td>
</tr>
<tr>
<td><strong>Differential (x10⁹/L)</strong></td>
<td>Neutrophils 1.19</td>
</tr>
<tr>
<td></td>
<td>Lymphocytes 0.71</td>
</tr>
<tr>
<td></td>
<td>Monocytes 0.02</td>
</tr>
<tr>
<td></td>
<td><strong>Blasts 0.02</strong></td>
</tr>
<tr>
<td><strong>Hemoglobin (g/L)</strong></td>
<td>97</td>
</tr>
<tr>
<td><strong>MCV (fL)</strong></td>
<td>94</td>
</tr>
<tr>
<td><strong>Platelets (x10⁹/L)</strong></td>
<td>153</td>
</tr>
</tbody>
</table>

* Prior CBC normal

**IMPRESSION:**

Pancytopenia
Work-up of PANCYTOPENIA

**Risk Factors / Practice Points:**

**Multiple Cytopenias**

- **Blood Smear**
  - **Abnormal Cells Present?**
    - **NO**
      - **ANC < 1.5 x 10^9/L?**
        - **NO**
          - Likely reactive / non-neoplastic due to drugs, critical illness, infections, connective tissue disease
            - Detailed History & Physical with particular attention to rule out ETOH / Cirrhosis
            - Referral to CCMB Hematology if persistent / symptomatic cytopenia
        - **YES**
          - Referral to CCMB Hematology for Suspected Home Malignancy, Dysplasia or AA
    - **YES**
      - **If Blasts, NRBC, Dysplasia or Immature WBC**
        - URGENT Referral to CCMB Hematology for Suspected Home Malignancy, Dysplasia or AA
      - **If Schistocytes**
        - EMERGENT Referral to CCMB for Suspected TTP or IUS

**Emergent Referral**

Page Hematologist On-Call
Required for the following:
- **ANC < 0.5 x 10^9/L**
- **Plt < 20 x 10^9/L**
- Symptomatic anemia in the absence of bleeding or iron deficiency (usually Hb < 70g/L)
- Blasts or schistocytes seen on the blood film
Acute leukemia – Clinical manifestations

• Constitutional symptoms
• Fatigue, malaise
• Anemia (pallor, heart failure)
• Thrombocytopenia (bleeding)
• Leukopenia / leukocytosis (infection)
Acute leukemia - Diagnosis

• Leukocytosis (blasts) OR pancytopenia
  – Peripheral blood OR bone marrow blasts >20%

• Delayed treatment is associated with reduced survival
• Early mortality related to bleeding and infection

Sekeres, Blood, 2009
Walter, JCO, 2011
Diagnosis – Take home points

• Present with constitutional symptoms, infections, bleeding
• CBC can show leukocytosis OR pancytopenia
• Differential and peripheral film are very informative

• New blasts are always bad; call HEMATOLOGY ON CALL
Acute leukemia - Complications

- White blood cells (infection, leukostasis)
- Hemoglobin (symptomatic anemia, CHF)
- Platelets (bleeding)
- DIC (bleeding, thrombosis)
- Tumor lysis syndrome
Acute leukemia - Assessment

• History & physical
  – Focal infection
  – Bleeding (intracranial, GI, mucocutaneous)
  – Thrombosis (DVT, PE)
  – Organ dysfunction (head to toe)
    • Leukostasis
Acute leukemia - Assessment

• Laboratory tests
  – CBC, differential, blood film
  – Electrolytes, Ca/Mg/PO4, albumin
  – Creatinine
  – Liver enzymes
  – LDH, uric acid
  – DIC screen (INR, aPTT, fibrinogen, d-dimer)
Case #2 / #3 Revisited

• Both patients were transferred to HSC leukemia service within 24 hours
• Baseline investigations (bone marrow, MUGA)
• Started induction chemotherapy
Take home messages

• TTP and acute leukemia are medical emergencies with acute life-threatening complications
• Maintain a high index of suspicion
  – TTP – anemia / thrombocytopenia
  – Acute leukemia – leukocytosis / pancytopenia
• If you suspect these, please call hematology on-call (at any hour!)
Thank you

bhouston@cancercare.mb.ca
lminuk@cancercare.mb.ca