Dysplastic Features and Malignant Cells in Blood and Bone Marrow

BCSLS Bone Marrow Workshop 2017
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Outline

• Dysplastic features in blood cells

• Abnormal cells in blood/bone marrow
  – Blasts and their variants
  – High grade lymphoma cells
  – Plasma cells

• Case examples, caveats
Myelodysplastic Syndromes (MDS)

- Peripheral blood cytopenias + dysplasia in one or more of cell lines + ineffective hematopoiesis

- Increased risk of development to acute myeloid leukemia
Erythroid dysplasia (peripheral blood)

- Macrocytic anemia
- Anisopoikilocytosis
- Basophilic stippling
- Dimorphic RBC pop
- Pappenheimer bodies
- Teardrop cells
- Howell-Jolly bodies
Erythroid series (bone marrow)
Erythroid dysplasia

- Erythroid hyperplasia
- Megaloblastoid changes
- Multinuclearity
- Nuclear pycnosis
- Nuclear lobulation
- Cytoplasmic fraying
- Ferritin sideroblast
- Ring sideroblasts
Granulocytic Dysplasia

Normal neutrophil

Pseudo-Pelger anomaly

Abnormal nuclear shape

Hypo-degranulation

Blood 2013 122:4021-4034
Megakaryocytic dysplasia

Normal megakaryocyte

Micromegakaryocyte

Multiple separated nuclei

Small binucleated cell

Monolobal cell
Exercise: What signs of dysplasia can you spot here?
What dysplasia can you spot here?
Important points

• !!! Assess CBC, blood film, bone marrow aspirate/biopsy
  – Dysplasia, increased blasts

• Collect specimens for:
  – Flow cytometry; if increased blasts – acute leukemia panel
  – !! Cytogenetics
  – Molecular genetics (0.5 ml fresh marrow aspirate in unopened in EDTA tube! Up to 6 days old)
Important points

- Cytopenia (s) present
- Dysplasia >10% of the cells in affected lineage (s)
- Blasts <20% (otherwise AML)
- !Perform:
  - Iron stain (for ring sideroblasts)
  - Reticulin stain for fibrosis
  - Potentially useful IHC: CD34, 117, CD61 and glycophorin
Case

- 81 F with transfusion-dependent anemia
- Hb 78, MCV 93, retic 34
- WBC 3.0 (neut 0.9, lymph 1.2, mono 0.7, eos 0.0)
- Platelets 224
- **Cytogenetics**: normal female karyotype
- **Diagnosis**: Refractory Cytopenia with Multilineage Dysplasia (RCMD) with Ring Sideroblasts (MDS WHO 2008 classification)
Malignant cells in blood and bone marrow
CLUES TO SUSPECT ACUTE LEUKEMIA in CBC and BLOOD FILM

STEP 1:

Abnormalities of CBC:
Look for signs of marrow failure such as anemia, neutropenia and thrombocytopenia
- Pancytopenia usually present in AML (acute myeloid leukemia)
- CBC could may be relatively preserved in ALL (acute lymphoblastic leukemia)

STEP 2:

a) Assess for blasts/blast equivalents:
   Circulating blasts could vary from low to high

b) Look for dysplastic features: Most commonly associated with AML.
Blasts

• Large nucleus, finely dispersed chromatin, variably prominent nucleoli

• Relatively high nuclear/cytoplasmic ratio

• Variable number of cytoplasmic granules, may be concentrated in limited portion of cytoplasm

• Auer rod(s) are characteristic of AML
### Blasts: AML vs ALL

<table>
<thead>
<tr>
<th></th>
<th>AML</th>
<th>ALL</th>
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<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Medium to large</td>
<td>Variable small to medium</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td>Fine granules may be present</td>
<td>Usually scant</td>
</tr>
<tr>
<td><strong>Auer rods</strong></td>
<td>Present in 60-70% cases</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Chromatin</strong></td>
<td>Fine</td>
<td>Fine to moderately condensed</td>
</tr>
<tr>
<td><strong>Other cells</strong></td>
<td>Can have dysplastic changes in myeloid cells</td>
<td>Myeloid cells are usually not dysplastic</td>
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Acute promyelocytic leukemia (M3)

- Blast equivalent in APL only:
  - Nuclear chromatin is more condensed
  - Intense cytoplasmic granularity is usually present (pinkish cytoplasmic hue)
  - Nuclear configuration is variable, but nuclear folding and lobulation are characteristic of microgranular variant of APL

NOTE:
- Classic APL is usually associated with profound neutropenia and thrombocytopenia, and occasional circulating APL blasts.
** Make 2 or more blood films and scan slides thoroughly.**
- Microgranular variant of APL has typically high WBC.
AML with inv(16) (M4Eo):
- Monocytic blasts
- Eosinophils show dense granulation
Blasts = high N/C ratio? Not always!

Acute monoblastic/monocytic leukemia (M5)
Other types of blasts

Microblasts

Megakaryoblasts
Erythroblasts in Acute Erythroid Leukemia (M6)

Pic courtesy of Dr. Hudoba

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Acute Erythroid Leukemia (cont’d…)

Pics courtesy of Dr. Hudoba
Blast “mimics”

Circulating High Grade Lymphoma Cells (DLBCL)

Blastoid variant of Mantle Cell Lymphoma
Burkitt’s lymphoma/leukemia vs Acute Erythroid Leukemia
Important points

• Assess CBC, blood film thoroughly for blast morphology.
  – Sometimes only rare blasts can be found in peripheral blood (e.g. APL).
  – Beware of blast mimics!
  – Refer CBC/slide to Hematopathologist ASAP

• Bone marrow aspirate/biopsy → collect sample for:
  – Flow cytometry
  – Cytogenetics
  – Molecular genetics (0.5 ml fresh marrow aspirate in unopened in EDTA tube! Up to 6 days old)
What are these cells?

Plasma cell leukemia
Case

- 63 y/o F
- Fatigue, confusion, “unsteadiness”
- ++ Hypercalcemia (Ca = 4.8)
- Renal failure (Cr 156)
- Multiple lytic lesions throughout bony skeleton (+ L3 compression fracture), pelvic mass
- Elevated serum IgE (5566 ug/L)
- Excess kappa free light chains (K/L ratio 4)
- ?? Plasma cell myeloma
• Hb : 108 (MCV 86)
• WBC: 17.7 (Neut 8.13, Lymph 6.18, Mono 3.18)
• Platelet: 79
• LDH: 3388 !!
• Liver enzymes (AST 60, ALT 120, GGT 597, ALP 350, Bili 11)
Blood smear
Bone Marrow Aspirate
• **IHC:** CD20+, BCL2+, CD10-

• **Flow cytometry:**
  – Negative for: CD5, CD10, CD23 and Tdt.

• **Diagnosis?** DIFFUSE LARGE B CELL LYMPHOMA.
KEEP CALM
ITS QUIZ TIME