e-Learn Lab — Hematology

Based on IQMH Centre for Proficiency Testing Survey MORP 1901-SB
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Focus of this Presentation

• This is a hematology morphology case study.
• You will be presented with patient information and photomicrographs and will be given information about the case for the purpose of self-learning.
Case discussion and photomicrographs provided by the members of the IQMH Hematology Scientific Committee and the IQMH Consultant Technologist.
Patient Information

- 46-year-old female, admitted with lower back pain (osteoporosis) and fever
- Past medical history of rhabdomyosarcoma (age 6)
- Treated with Adriamycin, Vincristine and Cyclophosphamide
# Laboratory Data

<table>
<thead>
<tr>
<th>Complete Blood Count</th>
<th>Reference Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count</td>
<td>$3.8 \times 10^9$/L</td>
</tr>
<tr>
<td></td>
<td>$4.0–11.0 \times 10^9$/L</td>
</tr>
<tr>
<td>Erythrocyte count</td>
<td>$3.87 \times 10^{12}$/L</td>
</tr>
<tr>
<td></td>
<td>$4.00–5.10 \times 10^{12}$/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>116 g/L</td>
</tr>
<tr>
<td></td>
<td>120–160 g/L</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.365 L/L</td>
</tr>
<tr>
<td></td>
<td>0.350–0.450 L/L</td>
</tr>
<tr>
<td>MCV</td>
<td>94.3 fL</td>
</tr>
<tr>
<td></td>
<td>80.0–100.0 fL</td>
</tr>
<tr>
<td>MCH</td>
<td>30.0 pg</td>
</tr>
<tr>
<td></td>
<td>27.5–33.0 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>318 g/L</td>
</tr>
<tr>
<td></td>
<td>305–360 g/L</td>
</tr>
<tr>
<td>Platelet count</td>
<td>$77 \times 10^9$/L</td>
</tr>
<tr>
<td></td>
<td>$150–400 \times 10^9$/L</td>
</tr>
<tr>
<td>MPV</td>
<td>10.1 fL</td>
</tr>
<tr>
<td></td>
<td>8.0–13.0 fL</td>
</tr>
</tbody>
</table>
# Laboratory Data - Differential

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Result *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils (bands and segmented)</td>
<td>$1.1 \times 10^9$L</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>$0.8 \times 10^9$L</td>
</tr>
<tr>
<td>Monocytes</td>
<td>$0.1 \times 10^9$L</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>$0.3 \times 10^9$L</td>
</tr>
<tr>
<td>Blasts/Blast Equivalents</td>
<td>$1.5 \times 10^9$L</td>
</tr>
<tr>
<td>Nucleated Erythrocyte Count</td>
<td>2/100 Lkc</td>
</tr>
</tbody>
</table>

* As reported by five referees
Peripheral Blood Image 1

Wright-Giemsa stain, ×40 magnification
Peripheral Blood Image 2

Wright-Giemsa stain, ×40 magnification
Think about the morphological features and a possible diagnosis before moving to the next slide.
Key Morphological Findings

- Blasts/blast equivalents
- Auer Rods
Patient Diagnosis

Acute myeloid leukemia
• The main morphologic feature is the presence of blast cells, some with Auer rods.
• The blasts are medium in size with scant to moderate amounts of cytoplasm with azurophilic granules and occasionally Auer rods.
• In addition to blast cells, the neutrophils also showed dysplastic changes predominately hypogranulation but also hypolobation.
Discussion

• Blast cells are precursors to mature circulating blood cells.
• They are found in small numbers in the bone marrow and are not found in the peripheral blood of healthy individuals.
• No single morphologic characteristic identifies a blast cell.
Discussion

• In general, blasts are medium to large in size with a large nucleus with immature chromatin, a prominent nucleolus, and scant cytoplasm with or without cytoplasmic granules.

• The morphology of myeloid blast cells is heterogeneous depending on the leukemia cell line and the stage of maturation.

• Despite the cell line of origin, myeloid blast cells often exhibit features indicative of their myeloid lineage including cytoplasmic granules or isolated Auer rods.
Discussion

• Auer rods are pink, needle-like cytoplasmic structures comprised of aggregated cytoplasmic granules.

• The presence of Auer rods is specific to the myeloid lineage and are not a morphologic feature of reactive or neoplastic lymphocytes.
Differentiation From Reactive Lymphocytosis

• Reactive lymphocytosis is most often due to a viral infection.
• Other causes also include but are not limited to bacterial or parasitic infections, autoimmune disorders, smoking, or stress.
• Reactive lymphocytosis has pleomorphic morphology, meaning all cells tend to be different sizes and shapes.
Differentiation From Reactive Lymphocytosis

- Classic reactive lymphocytosis due to a viral infection will often involve small, round lymphocytes (i.e.: classic lymphocyte morphology) in addition to intermediate to large lymphocytes with abundant pale blue or basophilic cytoplasm that “hugs” the red cells.

- The American Society of Hematology Image Bank is a useful resource for examples of reactive and neoplastic lymphocyte morphology.
Differentiation From Reactive Lymphocytosis

- Sometimes the larger lymphocyte forms will have azurophilic granules indicating large granular lymphocytes.
- Large granular lymphocytosis is commonly seen with viral infections, as a reaction to malignancy, or after chemotherapy treatment.
- This heterogeneous morphology in addition to the clinical history are often helpful clues when deciding if the lymphocytosis is pathologic.
Differentiation From Neoplastic Lymphocytosis

- Neoplastic lymphocytosis occurs due to a lymphoproliferative disorder involving the bone marrow.
- Neoplastic lymphocytosis is often monomorphic, meaning all the neoplastic cells tend to be the same size and have similar features.
- The blood film will often show a population of normal lymphocytes in addition to a monomorphous population of neoplastic lymphocytes.
Differentiation From Neoplastic Lymphocytosis

- Similar to blast cells, no single morphologic characteristic identifies a neoplastic lymphocyte.
- However, common features include folded, cleaved, or convoluted nuclei with compact chromatin, cytoplasmic projections, or prominent nucleoli.
- Sometimes neoplastic lymphocytes will have azurophilic granules, but Auer rods are not a morphologic feature of reactive or neoplastic lymphocytes.
Discussion

• Acute myeloid leukemia is a heterogeneous clonal hematopoietic malignancy whereby immature hematopoietic cells proliferate in the bone marrow, peripheral blood, and other tissues.

• The uncontrolled proliferation of immature hematopoietic cells results in bone marrow failure and patients often present with signs and symptoms related to their cytopenias.
Discussion

- Incorporation of multiple diagnostic criteria is needed in order to diagnose and classify hematopoietic disorders.
- The World Health Organization (WHO) Classification of Tumours of Haematopoietic and Lymphoid Tissue is an international diagnostic standard that incorporates several diagnostic criteria including clinical features, morphology, immunophenotype, and genetics.
- The bone marrow morphology of the current case confirmed acute myeloid leukemia with myelodysplastic changes in a patient with previous exposure to cytotoxic chemotherapy.
Discussion

• Acute myeloid leukemia with myelodysplasia related changes (AML-MRC) is a specific entity in the WHO classification and is often associated with poor prognosis.
• However, not all AMLs with dysplasia fit into this category.
• Cases of AML with mutations of NPM1 or biallelic mutation of CEBPA can often show dysplastic features but are not included in AML-MRC.
Discussion

• The clinical history indicated this patient had previous exposure (40 years ago) to cytotoxic chemotherapy as well as radiation.

• Therapy related AML is also a designated disease entity in the WHO and can occur as a late complication of cytotoxic chemotherapy or radiation treatment.

• It commonly presents 5-10 years after exposure and often involves unbalanced loss of genetic material, commonly loss of material from chromosome 5 or 7, loss of TP53, or a complex karyotype.
Discussion

• Molecular testing confirmed this patient has AML with biallelic CEBPA gene mutation.
• The revised 4th edition of the WHO includes this entity in a category called “Acute myeloid leukemia with gene mutations”.
• The CEBPA gene codes for a transcription factor that plays an important role in myeloid differentiation.
Discussion

• This mutation is seen in up to 10% of AML cases although a patient must have two mutations (one in both alleles) of this gene in order to be diagnosed in this category.

• Acute myeloid leukemia with biallelic mutation of CEBPA often presents de novo.

• This entity does not have any characteristic morphology although multilineage dysplasia is seen in approximately 26% of cases and does not have any prognostic significance.
• Most cases have morphologic features similar to those of AML with or without maturation. The blast cells express CD34 in addition to typical myeloid antigens (CD13, CD33, and CD15).

• CD7 is expressed in 53-70% of cases.

• This sub-type of AML is generally associated with a favourable prognosis.
Blast cells, reactive lymphocytes, and neoplastic lymphocytes are relatively common blood film findings. Familiarity with their morphologic differences and appropriate classification has an important impact on patient diagnosis.


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