e-Learn Lab — Hematology

Based on IQMH Centre for Proficiency Testing Survey MORP 1910-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.
17-year-old female admitted to the pediatric intensive care unit with history of upper respiratory tract infection.

She developed toxic shock syndrome and septic shock.
# Laboratory Data

<table>
<thead>
<tr>
<th>Complete Blood Count</th>
<th>Reference Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count</td>
<td>8.9 × 10^9/L</td>
</tr>
<tr>
<td></td>
<td>3.5–10.5 × 10^9/L</td>
</tr>
<tr>
<td>Erythrocyte count</td>
<td>4.47 × 10^{12}/L</td>
</tr>
<tr>
<td></td>
<td>3.90–5.00 × 10^{12}/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>121 g/L</td>
</tr>
<tr>
<td></td>
<td>108–133 g/L</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.359 L/L</td>
</tr>
<tr>
<td></td>
<td>0.334–0.404 L/L</td>
</tr>
<tr>
<td>MCV</td>
<td>80.3 fL</td>
</tr>
<tr>
<td></td>
<td>76.0–90.0 fL</td>
</tr>
<tr>
<td>MCH</td>
<td>27.1 pg</td>
</tr>
<tr>
<td></td>
<td>24.8–30.2 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>337 g/L</td>
</tr>
<tr>
<td></td>
<td>320–360 g/L</td>
</tr>
<tr>
<td>Platelet count</td>
<td>71 × 10^9/L</td>
</tr>
<tr>
<td></td>
<td>130–380 × 10^9/L</td>
</tr>
<tr>
<td>MPV</td>
<td>11.8 fL</td>
</tr>
<tr>
<td></td>
<td>9.0–14.0 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>7.2 x 10^9 L</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>1.4 x 10^9 L</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0.3 x 10^9 L</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.1 x 10^9 L</td>
</tr>
</tbody>
</table>

* As reported by five referees
Peripheral Blood Image 1

Wright-Giemsa stain, ×100 magnification
Peripheral Blood Image 2

Wright-Giemsia stain, ×100 magnification
Think about the morphological features and a possible diagnosis before moving to the next slide.
Key Morphological Findings

- Neutrophils exhibiting Pelger-Huët forms
- Neutrophil vacuolation
- Echinocytes (burr cells)
Patient with toxic shock syndrome and septic shock. Leukocyte morphology exhibited neutrophil predominance with the presence of Pelger-Huët forms.
• Pelger-Huët type neutrophils classically show a bilobed nucleus with the lobes separated by a thin filament.¹

• This contrasts with normal neutrophils that typically have 3–4 nuclear lobes.
Discussion

• True Pelger-Huët anomaly (PHA) is a relatively rare hereditary disorder of nuclear segmentation, related to mutations in the lamin B receptor (LBR) gene.²
• Lamin B receptor is a component of the neutrophil nuclear membrane and is required for normal neutrophil morphological development.
• Most patients with PHA have heterozygous LBR mutations with their neutrophils displaying the characteristic bilobed appearance.
• In the very rare circumstance where patients have a homozygous LBR mutation, most neutrophils are monolobated.
• More frequently, other clinical conditions can result in pseudo-Pelger-Huët cells.
• These are neutrophils that resemble true Pelger-Huët cells but arise due to an acquired rather than congenital disorder.
• Pseudo-Pelger-Huët cells may be observed in myeloid disorders including myelodysplastic syndrome (MDS), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), various infections including HIV, tuberculosis, influenza, Mycoplasma pneumoniae and other severe bacterial infections, as well as various drugs including sulfonamides, colchicine, valproic acid, mycophenolate mofetil and tacrolimus.¹,²
Discussion

• As such, it is clinically important to distinguish true PHA from pseudo-Pelger-Huët cells. Careful review of the clinical history is important to identify any potential causes for pseudo-Pelger-Huët cells.

• If prior blood film reviews have identified normal appearing neutrophils, this essentially excludes true PHA.

• Various morphological features can also aid in distinction.
Discussion

• The presence of toxic changes (Döhle bodies, toxic granulation, vacuolation) raises the likelihood of infection, although these changes may also be seen in true PHA with concomitant infection/inflammation.

• If there is significant heterogeneity in the nuclear lobation of neutrophils, this is more in keeping with pseudo-Pelger-Huët cells.

• Particularly in MDS, other features of myelodysplasia may be observed including hypogranulation and increased nuclear/cytoplasmic ratio of granulocytes.
Discussion

- As well, the nuclear chromatin will not be as condensed and dark as in PHA.\(^2\)
- Given the above features, it is vital to have well-prepared and well-stained peripheral blood films.
- The blood films should be made as soon as possible after collection as specimens older than 12 hours may show neutrophil degeneration with round pyknotic nuclei, adding another layer of difficulty into the morphological assessment.\(^3\)
Discussion

• In this particular case, it is difficult to clearly distinguish between PHA with coexisting infection and pseudo-Pelger-Huët cells as a result of sepsis without more clinical history.

• Nonetheless, there was variation in neutrophilic morphology, including some normal lobated forms (not shown in the images provided), which favours the latter.

• The echinocytes observed in this smear are likely to be artefactual (prolonged exposure to EDTA) given the extremely high number although a component of renal dysfunction cannot be excluded.
Neutrophils with Pelger-Huët nuclei may be seen in both congenital and acquired conditions.

Assessment of morphological features on well-prepared and well-stained blood films in context of the clinical history is required for distinction between Pelger-Huët anomaly and conditions with pseudo-Pelger-Huët cells.


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