Case # 51
Peripheral blood smear from a dog

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Signalment and history

- 8-year-old, M/N, Weimaraner
- Presented for a possible splenic mass
- Lethargic and anorexic for 3 days
- Physical exam:
  - Bright, alert, responsive and energetic
  - T 102.9F, Pulse 120/minute, Panting, CRT <2sec
  - Enlarged mandibular lymph nodes (right>left)
  - No abnormalities on abdominal palpation
<table>
<thead>
<tr>
<th>CBC</th>
<th>Patient’s values</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct (%)</td>
<td>30.3 ↓</td>
<td>37 – 55</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>70.3</td>
<td>60 – 77</td>
</tr>
<tr>
<td>MCHC (g/dL)</td>
<td>33.8</td>
<td>32 – 36</td>
</tr>
<tr>
<td>Reticulocytes (/μL)</td>
<td>86,100 ↑</td>
<td>0 – 60,000</td>
</tr>
<tr>
<td>Platelets (/uL)</td>
<td>74,000 ↓ / clumped</td>
<td>164,000 – 510,000</td>
</tr>
<tr>
<td>MPV (fL)</td>
<td>24.1 ↑</td>
<td>8.4 – 13</td>
</tr>
<tr>
<td>WBC (/μL)</td>
<td>64,400 ↑</td>
<td>6,000 – 17,000</td>
</tr>
<tr>
<td>Neutrophils (/μL)</td>
<td>5,796</td>
<td>3,000 – 11,400</td>
</tr>
<tr>
<td>Lymphocytes (/μL)</td>
<td>52,808 ↑</td>
<td>1,000 – 4,000</td>
</tr>
<tr>
<td>Monocytes (/μL)</td>
<td>5,796 ↑</td>
<td>150 – 1,350</td>
</tr>
</tbody>
</table>
Leukocyte scattergram from Advia120

- Lymphocytes
- Large unstained cells

- Mononuclear cells
- Lysis-resistant cells
Blood smear
Blood smear
• Abdominal ultrasound
  - Enlarged liver with variable echogenicity
  - Enlarged spleen with normal echogenicity

• Cytology
  - Multiple organ involvement of neoplastic LGLs
  - Bone marrow, liver, spleen and left mandibular lymph node

• Diagnosis
  Large granular lymphocyte (LGL) leukemia/lymphoma (stage V)
Large granular lymphocytes (LGLs)

• Unique morphologic features:
  – Cytoplasmic azurophilic granules
    - At least 3 granules, 0.5µm or greater in diameter
  – Contain a variety of enzymes and substances
  – Induce cell death
Enzymes

• Perforin
  - 534 aa, MW 60,000 kDa
  - Form transmembrane channels
  - Facilitate delivery of toxic substances (granzymes)

• Granzymes
  - Serine proteases
  - Many subgroups; A and B are the major components

  Granzyme A
  - Cause cell death by caspase independent pathway

  Granzyme B
  - Cause apoptosis by various pathways
  - Directly activate caspase 3
  - Mitochondrial pathway through Smac/DIABLO
Cell types

• Cytotoxic T cells
  – αβ T cells and γδ T cell
  – Express CD3/TCR complex and CD8

• NK cells
  – Do not express TCR and have germline configuration of T cell receptor genes
  – No commercially available markers to detect NK cells in dogs

• Morphologically similar

• Most canine LGL leukemia originates from spleen
  – Express leukointegrin αdβ2 (CD11d)
  – Almost exclusively on the cells in the red pulp

• Bone marrow involvement is only seen in advanced stages
LGL leukemia in people

Clinical course varies depending on the cell type

• Cytotoxic T cell LGL leukemia
  - Slow progressive disease
  - Treatment is generally required only when clinical signs, anemia or neutropenia become evident

• NK cell LGL leukemia
  - Aggressive disease
  - Resistant to most chemotherapy protocols
  - Poor prognosis

LGL leukemia in dogs
Clinical course has not been evaluated based on the cell type
  - Poor prognosis
  - Respond poorly to chemotherapy
Case Summary

• LGL leukemia/lymphoma (stage V)
  - 3 days clinical history, but the disease may have been progressing over time
  - Initially responded to chemotherapy but lost to follow-up 6 months after presentation

• If additional phenotypic markers become available, differentiation of cell types may aid in the evaluation of therapies
Acknowledgements

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• Clin Path Lab technicians

Questions?
References