Hematology Case Challenges

Or, Maybe Not?

The Splenic Mass

Sadie

- 7 year old, female, spayed golden retriever
- Presentation (Emergency)
  - Episodic weakness (twice) over 2 week period
  - Acute collapse day of presentation, but recovered

Physical Exam Findings

- Pale mucus membranes, tachycardia (120 BPM)
- CRT prolonged @ 4 sec.
- Abdominal distension
  - Effusion and/or mass was difficult to determine on abdominal palpation
- PCV 19%
- TPP 5.4
- Plan: CBC
CBC Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value / Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>19.1 (6.0 – 17.0) x 10³</td>
</tr>
<tr>
<td>Neuts</td>
<td>15.2 (3.0 – 11.5) x 10³</td>
</tr>
<tr>
<td>Bands</td>
<td>0.900 (0.0 - 0.3) x 10³</td>
</tr>
<tr>
<td>Lym.</td>
<td>0.700 (1.0 – 4.8) x 10³</td>
</tr>
<tr>
<td>Mon.</td>
<td>2.3 (0.15 – 1.35) x 10³</td>
</tr>
<tr>
<td>Eos.</td>
<td>0.0 (0.1 – 1.25) x 10³</td>
</tr>
<tr>
<td>RBC</td>
<td>2.51 (5.4 – 7.8) x 10⁶</td>
</tr>
<tr>
<td>HGB</td>
<td>6.8 (13.0 – 19.0) g/dL</td>
</tr>
<tr>
<td>HCT</td>
<td>18.2 (37.0 – 54.0) %</td>
</tr>
<tr>
<td>MCV</td>
<td>76.2 (66 – 75) fl</td>
</tr>
<tr>
<td>MCHC</td>
<td>36.3 (34.0 – 36.0) g/dL</td>
</tr>
<tr>
<td>Plts</td>
<td>25.0 (150 – 430) x 10³</td>
</tr>
</tbody>
</table>

Reticulocyte count = 150,600 / µl (>80,000 = regenerative)

Blood film evaluation

Findings from Blood Film Evaluation

- Regenerative anemia (polychromasia high reticulocytes)
- Poikilocytosis
  - Acanthocytes
  - Schistocytes
- Thrombocytopenia!
- No large central palor!
- Not iron deficient!

Schistocytes

- Hallmark of fragmentation hemolysis
- Fragmentation of cells passing through tortuous or abnormal vessels
  - DIC
  - Neoplasia (HSA, Thyroid ACA)
    - Up to 50% of dogs with HSA
  - Vasculitis
  - Thromboembolism (Cushing-s, HWD)
  - Caval Syndrome
  - Glomerulonephritis
- Increased fragility of erythrocytes
- severe iron deficiency anemia
Abdominal Ultrasound

- Free abdominal fluid
- Large mass in cranial abdomen (14 cm)
  - Cavitated with mixed echogenicity
  - Appeared to be associated with the spleen

What is your working diagnosis?

1. Hemangioma
2. Hemangiosarcoma
3. Splenic torsion or vascular thrombosis
4. Hematoma
5. Lymphoma

No firm diagnosis?

- Hemangioma, hemangiosarcoma, hematoma, lymphoma?
  - Imaging not always helpful
- Hematological abnormalities indicate HSA
  - Anemia seen in 80% of dogs with splenic HSA
  - Dogs with splenic masses and evidence of anemia, fragmentation hemolysis and thrombocytopenia
  - Significantly greater risk of having HSA (90%)

Fine-needle Aspiration of Splenic Mass

- Potential for definitive, presurgical diagnosis
- Potential for complications
  - Seeding the abdomen with tumor cells
  - Hemorrhage
  - Ultrasound guided aspirate with 25 gauge needle
  - Stay away from cavitated areas of mass
Plan for Sadie

- Owners elected surgery and chemo if possible
- Sadie was transfused (PCV 26%)
- Surgery was performed and a 14 cm x 16 cm mass was identified in the spleen
- Multiple, red-purple, raised nodules were present in all lobes of the liver
- The spleen and biopsies taken from the hepatic masses were submitted for histopathology
- Final Dx: hemangiosarcoma

Treatment

- Chemotherapy was initiated approximately 1 week post-op (once histopath confirmed a diagnosis) (PCV 35%)
- 21 day cycle of VAC
  - Vincristine 0.75 mg/m² BSA (IV) (Day 8 & 15)
  - Doxorubicin 30 mg/m² BSA (IV) (Day 1)
  - Cyclophosphamide 200 - 300 mg/m² BSA (PO) (Day 10)
- Sadie received 4 cycles of therapy
**Prognosis**
- Long-term prognosis extremely poor
- Death from exsanguination from rupture of metastatic site
- Surgery alone rarely curative with MST of 1 to 3 months
- Multi-drug chemotherapy MST 6 to 9 months

**Sadie**
- Sadie was found dead in her bed 9 months after splenic surgery
- Likely the result of ruptured metastatic lesion

**Penny: 8 year old, F/S Long-haired Dachshund**

**Presentation to Referring Veterinarian**
- 3 week history of lethargy
- Eating and vomiting grass and grass roots
- Sleeping a lot
- Presently on monthly heartworm medication
- Vaccinations current
Penny’s Exam

- Temp. 101.5°F
- Respiration 35 PM
- HR 90 BPM
- Pale mucus membranes
  - No history of trauma or evidence of hemorrhage
- Fecal parasites check negative
- Heartworm test negative
- CBC & Biochemical profile

CBC Results

- HCT 12.2% (37-55)
- WBC 6.58 K/µl (5.5-16.9)
- RBC 2.0 M/µl (5.5-8.5)
- Neut 4.23 K/µl (2-12)
- Hgb 4.9 g/dl (12-18)
- Lym 1.52 K/µl (1.0-4.9)
- MCV 62.0 fl (60-77)
- Mono 0.67 K/µl (0.3-2.0)
- MCH 24.5 pg (18-30)
- Eos 0.13 K/µl (0.1-1.5)
- MCHC N/A
- Baso 0.04 K/µl (0-0.1)
- RDW 15.9% (14.7-17.9)
- Platelet 819 K/µl (175-500)

- Reticulocyte 0.6%
- Absolute retic 11.6 K/µl
Biochemical Profile

- WNL

Problem List

- Severe nonregenerative anemia
- Thrombocytosis
- Pica
- Vomiting
- Plan
  - Refer to UF-VMC for further evaluation

Problem List

- Severe nonregenerative anemia
- Thrombocytosis
- Pica
- Vomiting
- Plan

Penny’s Presentation

- 1 month history of lethargy and decreased appetite
- Eating grass and grass roots and vomiting them
- Physical exam
  - BW 4.6 kg
  - Quite but alert
  - Temp 102.1
  - HR 80, Resp. 32
  - MM white with no CRT available
- Normal fecal color
- Fecal occult blood test (Hemocult) negative
Diagnostic Plan

- MDB
- CBC, UA, Biochemical profile
- Reticulocyte count
- Coombs’ test
- Cross match

CBC Results

- HCT 15.1% (37-55)
- WBC 6.92 K/µl (6.0-17)
- RBC 2.31 M/µl (5.4-7.8)
- Neut 4.5 K/µl (2-12)
- Hgb 5.4 g/dl (13-19)
- Bands .21 K/µl (0-.3)
- MCV 66.4 fl (66-75)
- Lym 1.80 K/µl (1.0-4.9)
- MCH 23.4 pg (18-30)
- Mono 0.45 K/µl (0.3-2.0)
- MCHC 35.8 g/dl (34-36)
- Eos 0.1 K/µl (0.1-1.5)
- RDW 12.1% (11-13)
- Baso 0.0 K/µl (0-0.1)
- Platelet 735 K/µl (150-430)
- Plasma Protein 6.9 g/dl
  - Reticulocyte 0.1%
  - Absolute retic 2.3 K/µl

Iron Levels

- Serum iron 374 ug/dl (70-264)
- TIBC 559 ug/dl (246-504)
- % saturation 67 (19-79)

Biochemical Profile

- If Penny was bleeding (e.g. chronic hemorrhage) what abnormality would you see in the profile?
  - Low total protein (albumin, pos. globulin)
  - High BUN, normal creatinine
- Penny was normal, no abnormalities seen
Diagnostic Plan

- Cross-matched transfusion
- Adapted to chronic anemia
- Concern for anesthesia
- General anesthesia
- Imaging
  - Thoracic and abdominal radiographs (neoplasia?)
  - Ultrasound of abdomen
- Bone marrow collection and evaluation

Results

- Pre transfusion PCV 15.1%
- Post transfusion PCV 20.0%
- Imaging: no abnormalities seen
- Bone marrow aspirate
  - Dry tap (Why?)
  - Core biopsy of marrow
    - Role core on slide for cytological evaluation
    - Submit core for histopathology
- Sent patient home awaiting biopsy results
Bone Marrow Evaluation

- Erythroid hyperplasia with left-shifting
- Maturation arrest at rubricyte/metarubricyte stage
- Erythrophagocytosis of precursor cells
- Tentative diagnosis: Nonregenerative (Central) immune-mediated anemia

Core Biopsy

- *Myelofibrosis*, multifocal, moderate
- Erythroid hyperplasia
- Hemosiderosis
- Megakaryocytic hyperplasia with left-shift

Tentative Diagnosis and Plan

- Nonregenerative IMA
- Direct Coombs’
- Tick titers
- Await results and begin therapy
Recheck
➢ Return visit 1 week after diagnostic evaluation
➢ Penny more active after transfusion, but getting lethargic again
➢ PCV 15% with low number of **spherocytes on blood smear**
➢ Direct Coombs’ negative at 1:2
➢ Serology for *E. canis* and *A. phagocytophilum* -negative

Treatment Plan
➢ Azathioprine 2mg/kg for two weeks
➢ Prednisone 1 mg/kg BID
➢ Famotidine 5 mg per day (pepcid AC)

2 week Recheck
➢ Penny more alert than before
➢ PCV 22%
➢ No spherocytes noted on smear
➢ Continue on current dose until PCV normal

Nonregenerative IMHA
➢ Estimated 33% to 58% of IMHA are nonregenerative
➢ Anemia typically severe, (**median PCV 11%**) with majority being <20%
➢ Age 10 mo. to 12 yr. (median 6.5 yr.)
➢ Female over-represented in most studies
➢ **Dachshunds over-represented at UF (>10 cases)**
➢ Two forms
  ➢ PRCA: more severe less common form
  ➢ Evidence of erythropoiesis in bone marrow (>90%)

Stokol et al., JAVMA 216:14291436, 2000. (43 cases)
**Chronicity of Anemia**
- Important in establishing diagnosis
- Most dogs have clinical signs of 7 or more days
  - Lethargy, anorexia, pallor, weakness, pica, vomiting
- Animals tolerant of very low red cell mass

**Laboratory Analysis**
- Normocytic, normochromic anemia
  - Spherocytes seen in small percent (16%), numbers vary
- 0 to 7 NRBC’s / 100 WBC (no / rare polychromasia)
- Normal leukocyte count
  - 50% had mild left-shift
- Platelets most often increased
  - Decreased in 22% of cases
- Direct Coombs’ test positive in 30 to 50% (low titer 1:4)
- ANA positive in 23%

**Bone Marrow Evaluation** *(Stokol et al.)*
- Bone marrows difficult to aspirate in 21 of 43 dogs
  - No spicules
  - Dry tap
- 16 dogs had core biopsies, all had myelofibrosis (reversible)
- Erythroid precursors may be absent (5% PRCA), normal numbers, or increased (most common)
- Erythroid hyperplasia was common among dogs with myelofibrosis
- Maturation arrest at rubricytes and metarubricytes with few to no polychromatophilic cells
- Most dogs had large amounts of iron

**Treatment for NRIMHA** *(Stokol, et al., JAVMA 216:1429-1436;2000)*
- Combination chemotherapy
  - Pred. & Cytoxan (73% remission)
  - Pred. & Azathioprine (52% remission)
  - Pred. alone (25% remission)
- Response rate
  - Complete remission (55%)
  - Partial remission (18%)
  - Poor response (27%)
Response Time and Mortality

- Response to treatment seen in 1 to 10 weeks
  - Median 2 weeks
- 18 cases with extensive follow-ups
  - 5 off all medication within 2 years
  - 9 on alternate day pred / azathioprine for 3 years
  - 6 relapsed when drug dosage / frequency was reduced
- If drugs are reduced, maintain at reduced level for prolonged period of time (60 days?)
- Mortality rate 28%

Summary

- NR-IMHA should be considered in dogs with severe, chronic, nonregenerative anemia
- Normal WBC and normal or increased platelets
- Bone marrow evaluation may aid in confirming diagnosis
  - Fibrosis, maturation arrest, erythrophagia
  - Myelofibrosis may complicate marrow aspiration
- Treatment should include combination chemotherapy
- Response to therapy may take weeks to months

The End?