Tyler

- 10 year old M(N) Doodle
- Acute onset vomiting x 2
- Lethargic on walk this morning

Tyler

- T 99.5°F
- HR 140 bpm
- RR 40
- Pale mm
- CRT 2 seconds
- Cool extremities
- Weak femoral pulses with deficits

Tyler’s ECG

Abdominocentesis

- 5 – 7 ml/kg

Stages of Shock

<table>
<thead>
<tr>
<th></th>
<th>Compensatory 15-30%</th>
<th>Early Decompensatory 30-40%</th>
<th>Late Decompensatory &gt; 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Increased</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Mucous Membranes</td>
<td>Hyperemic</td>
<td>Pale</td>
<td></td>
</tr>
<tr>
<td>CRT</td>
<td>Rapid</td>
<td>Prolonged</td>
<td></td>
</tr>
<tr>
<td>Pulse Quality</td>
<td>Normal to bounding</td>
<td>Normal to decreased</td>
<td>Weak</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Normal to increased</td>
<td>Normal to decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Core Temperature</td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
</tbody>
</table>

Oxygen Delivery

\[ \text{DO}_2 = Q \times C_aO_2 \]

\[ Q = \text{Heart Rate} \times \text{Stroke Volume} \]

\[ C_aO_2 = [1.34 \times \text{Hb} \times S_aO_2] + [0.003 \times P_aO_2] \]

Rapid Volume Resuscitation

- Start with \( \frac{1}{4} \) of the calculated “shock” dose, then reassess perfusion parameters
  - Heart rate
  - Blood pressure
  - Capillary refill time
  - Urine output

Treatment to Improve Oxygen Delivery

- Fluids
- Antiarrhythmics
- Crystalloids
- Colloids

\[ C_aO_2 = [1.34 \times \text{Hb} \times S_aO_2] + [0.003 \times P_aO_2] \]

- Inotropes
- Whole Blood
- Packed RBC’s
- Oxygen supplementation
**Rapid Volume Resuscitation**

- Helpful Hint
  - For dogs, take their body weight in POUNDS, and add a zero
  - This equals ¼ shock dose of fluids!

**Small Volume Resuscitation**

- Colloidal administration 5 ml/kg bolus
- Reassessment of perfusion parameters
- Used in:
  - Head trauma or closed cavity hemorrhage
  - Pulmonary contusions

**Circulation – Fluid Therapy**

- Large (shock) bolus dosing of crystalloid, hypertonic or colloid fluids can raise pressures to supernormal levels
- Newly formed clots to break off damaged vessels
- Dilutional coagulopathy

**Dysrhythmias**

**Treatment of Ventricular Tachycardia**

- 1 – 2 mg/kg IV over 1 – 2 minutes followed by 50 – 100 mcg/kg/min IV CRI


- PCV/TS
- Cytology?
- 163 peritoneal effusions
- Malignancy found 18%, > ½ carcinoma
- 64% sensitivity

* Presence of peritoneal effusion signifcantly associated with malignancy (p = 0.0007)


- Eliminating 1 view would change diagnosis in 12-15% of cases
- Both laterals more sensitive than 1 lateral and DV or VD

**Use of radiography in combination with computed tomography for the assessment of noncardiac disease in the dog and cat.** Vet Radiol Ultrasound 46(2):114-1221, 2005.

- 28 dogs, 5 cats
- Location/extent pathology, mediastinal involvement
- 4/33 no new information
- Change in diagnosis 16/33 (48%)


- 71 dogs with hemoabdomen, splenic mass and required transfusion
- 54/71 malignancy
- 50/54 (92.6%) HSA
- Lower platelet count
- Lower TS
- Negative predictive values of above not great


- 83 dogs with hemoabdomen
- 90% of bleeding isolated to spleen
- Massive transfusion negative prognostic indicator
- Splenic hemorrhage positive predictive indicator
- “Surgical intervention, regardless of etiology, resulted in discharge from hospital in 84% of dogs”.

**Hemoabdomen Study**

- Dogs with hemoabdomen and splenic mass
- Vascular endothelial growth factor (VEGF)
- Thymidine kinase
- Abdominal fluid
- Peripheral blood
- Splenic biopsy
“The Talk”

- Presence of hemoabdomen = malignancy 65-80%

Tyler

- T 99.5°F
- HR 110 bpm
- RR 40
- Pale mm
- CRT 1.5 seconds
- Warm extremities
- BP 100/60 (73)
- ECG Normal

Balanced Anesthesia

- Opioid + Benzodiazepene ± Etomidate

<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>5-10 mcg/kg IV</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.2-0.5 mg/kg IV</td>
</tr>
<tr>
<td>Diazepam</td>
<td>0.4 mg/kg IV</td>
</tr>
<tr>
<td>Etomidate</td>
<td>0.5 – 1.0 mg/kg IV</td>
</tr>
</tbody>
</table>

To surgery......

Surgical Indications for the Hemoabdomen

- failure to achieve stability of patient
- continued evidence of bleeding
- radiographic evidence of pneumoperitoneum, hernia or mass effect
- owner aware of prognosis
Preoperative concerns

- Hypovolemic shock
- Anemia
- Cardiac arrhythmias
- Coagulopathy
- Metastatic disease
- Concurrent injury if trauma indicated

Hemoabdomen – Surgical Preparation

- Prepare large area of ventral abdomen (xiphoid to pubis); paracostal access; prepare thoracic and inguinal regions if indicated
- Rapid access to the abdominal cavity
- An assistant, suction capability, radioopaque sponges and electrosurgical instruments are ideal

Hemoabdomen – Principles of Surgery

- Ventral midline incision
- Examine spleen, liver and kidneys first; if source of bleeding not found, proceed with systematic abdominal exploration

Hemoabdomen – Controlling hemorrhage

- Direct pressure to peripheral vessels
- Pack with laparotomy sponges
- Pringle maneuver
- Direct pressure to aorta (assistant)
- Aortic cross clamping
  - bulldog clamps
  - Rumel tourniquet

Hemoabdomen - Hemostasis Aids

- Suture
- Surgical staples
  - Thoracoadominal stapler (TA)
  - Ligate and divide stapler (LDD)
  - Surgiclip/Hemoclip
- Vessel sealing devices
  - Ligasure
  - EndSeal
- Hemostatic agents
  - Gelfoam
  - Surgicel
  - RAPID powder
  - Gels

Hemoabdomen - Spleen

- Lacerations can be sutured, omentalized or covered with Surgicel
- Total splenectomy most frequently done for both trauma and masses
Total splenectomy

- Most common
- Neoplasia
- Trauma
- Torsions
- Thrombosis

Arterial blood supply

- Splenic artery: 3-5 branches
- Supply to the left limb of the pancreas
- Short gastric arteries
- Left gastroepiploic artery

Total Splenectomy - Surgical technique

- Ventral midline incision
- Exteriorize the spleen
- Double ligate vessels at splenic hilus
- Preserve the short gastrics if possible

Splenectomy – Ligate Divide Stapler (LDS)

- Easy to use
- Faster than suture
- Staples are insecure and often slip
- Expensive compared to suture or hemoclips
- Comparable cost to Ligasure per use

Splenectomy using Hemoclips

- Easy to place
- Two on artery on side to stay
- One on vein on side to stay
- Relatively cheap compared to TA staples and vessel sealing
- Requires a lot hemoclips
- Relatively secure

Splenectomy - Ligasure

- Efficient
- Fast
- Seals vessels up to 7mm
- Minimal lateral thermal spread (<2mm)
- Expensive
**Hemoabdomen - Liver**

- Repair of superficial lacerations with suture or Gelfoam
- Liver lobectomy indicated for bleeding masses or irreparable hemorrhage isolated to a single lobe

**Partial Liver Lobectomy**

- Indicated when disease involves only a portion (peripheral) of the liver lobe

**Complete Liver lobectomy**

- Indicated for bleeding masses or irreparable hemorrhage isolated to a single lobe
- Double ligation of blood vessels and biliary ducts near the hilus
- Thoracoabdominal (TA) stapler
- Ligasure
- Finger fracture/suture

**Liver lobectomy – thoracoabdominal (TA) stapler**

**Liver lobectomy - TA stapler**

**Hemoabdomen - kidney**

- Direct pressure and repair attempted
- Nephrectomy reserved for uncontrollable hemorrhage, avulsion and neoplasia
Hemoabdomen – adrenal

- Rare
- Typically malignant when causing hemorrhage
- Difficult to control hemorrhage until adrenalectomy is complete

Thorough abdominal exploration is indicated once hemorrhage is controlled.

Prognosis is dependent on underlying etiology

<table>
<thead>
<tr>
<th>Traumatic</th>
<th>HEMOPERITONEUM</th>
<th>Non-traumatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt Trauma (HBC)</td>
<td>Penetrating trauma</td>
<td>Neoplasia</td>
</tr>
<tr>
<td>Spleen</td>
<td>Liver</td>
<td>Kidney</td>
</tr>
<tr>
<td>Mesenteric avulsion</td>
<td>Splenic</td>
<td>Hepatic</td>
</tr>
<tr>
<td>Renal Adrenal</td>
<td>Intestinal</td>
<td>Congenital</td>
</tr>
<tr>
<td>Toxin</td>
<td>DIC</td>
<td>Hepatobiliary disease</td>
</tr>
<tr>
<td>GDV</td>
<td>Splenic</td>
<td>Liver lobe torsion</td>
</tr>
</tbody>
</table>

Prognosis is dependent on underlying pathology

- Traumatic
  - Overall survival rate for dogs with severe traumatic hemoperitoneum was 57% in Mongi et al, JAAHA, 1995; After excluding those that were euthanized, survival rates for those treated medically and surgically were 75% and 67% respectively. Larger animals had a better prognosis. Presenting clinical signs, PCV (peripheral and effusion), pulse rate, site of intraabdominal hemorrhage and age did not correlate with survival.
  - Nodular splenic disease
    - 2 month post-op survival rate was 83% for dogs with non-neoplastic related hematomas and 31% for dogs with hemangiosarcomas (HSA) with or without associated hematomas, Spangler, Atlas, J Vet Intern Med, 1997
    - Median survival time of dogs with grade I or II splenic HSA treated by splenectomy alone was 86 days (range 14-470 days); Wood et al, JAAHA, 1998
    - HSA splenectomy alone results in median survival times of 19-65 days; dogs treated with surgery and chemotherapy have a median survival time of 143 days; Chun, Compendium, 1999

To the oncologist…..

Now what?

- Recheck 10-14 days after surgery
  - Remove sutures
  - Discuss diagnosis and overall prognosis
  - Review treatment options
- Important not to start injectable chemotherapy too soon after surgery
What types of neoplasia are seen with hemoabdomen?

- Splenic (MOST COMMON)
  - Hemangiosarcoma – prevalence of hemoabdomen higher in dogs with HSA compared to those with other tumors (80% vs. 20%)
  - Splenic stromal sarcomas (leiomyosarcoma, fibrosarcoma, other STS, undifferentiated sarcomas)
  - Fibrohistiocytic nodules
  - Lymphoma
  - Other
- Hepatic
  - Hepatocellular carcinoma (massive)
  - Hemangiosarcoma
  - Other (lymphoma, carcinomas, etc)
- Renal
  - Hemangiosarcoma
  - Other sarcomas
  - Renal cell carcinoma
  - Nephroblastoma
- Adrenal
  - Pheochromocytoma
  - Adrenocortical tumors
- Intestinal

Distribution of splenic masses with or without hemoperitoneum

<table>
<thead>
<tr>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multifocal tumor</td>
<td>67.6%</td>
</tr>
<tr>
<td>Hemangiosarcoma</td>
<td>15.4%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5.9%</td>
</tr>
<tr>
<td>Hematomas</td>
<td>3.7%</td>
</tr>
<tr>
<td>Renal tumors</td>
<td>2.4%</td>
</tr>
<tr>
<td>Heather</td>
<td>2.0%</td>
</tr>
<tr>
<td>Thoracic masses</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

What if histopathology is equivocal?

- Request immunohistochemistry
  - Hemangiosarcoma
    - von Willebrand’s Factor (factor VIII-related antigen)
    - CD31 (platelet endothelial cell-adhesion molecule – PECAM)
  - Sarcoma
    - Vimentin positive, negative for other markers
    - Round cell tumor
      - Lymphoma – CD3 (T-cell) or CD79a (B-cell) positive
      - Histiocytic sarcoma – CD18 positive, negative for other markers
      - Plasma cell – MUM1, CD79a, CD20, Pax5
  - Carcinoma
    - Cytokeratin
- REMEMBER TO SUBMIT ENTIRE SPLEEN!!!

Baseline Testing

- Is (re-)staging necessary?
  - Thoracic radiographs
  - Abdominal ultrasound
  - Echocardiogram
    - In dogs where echo was performed at diagnosis, only 3% had concurrent right atrial mass
    - Pre-chemotherapy screen
  - Biomarkers and monitoring treatment response
    - Thymidine Kinase
Thymidine kinase 1

- What is TK1
  - Cytosolic enzyme involved in DNA synthesis
  - Expression restricted to proliferating cells
- Use of TK1
  - Screening test for malignancy
    - Serum TK1 was significantly higher in HSA/other malignancy dogs vs. normal dogs
    - NOT different compared to dogs w/ benign splenic diseases
    - Very low TK1 (<1.55u/L) helps rule out splenic malignancy (especially HSA – 0/6 dogs had TK1 <1.55u/L)
    - Very high value does not rule in hemangiosarcoma!
  - Monitoring during therapy

Hemangiosarcoma – Systemic Tx options

- Injectable chemotherapy
- Immunotherapy
- Metronomic chemotherapy
- Alternative therapies
  - I’m Yunnity
  - Yunnan Baiyao

Splenic HSA – Treatment Options

- Splenectomy alone
  - MST 2-3 months (6.25% alive at 1 year)¹
- Splenectomy + injectable chemotherapy
  - Adriamycin alone
    - Q3 week protocol → MST 6 months²
    - Stage II dogs → 2 months
  - Q2 week protocol (dose intensified)³
    - Stage I dogs → 6 months
    - Stage II dogs → 3 months
  - With Gemcitabine → MST 8 months
    - Stage II dogs → 5 months
  - Pegylated liposomal encapsulated Adriamycin
    - No improved survival compared to free Adriamycin³
  - Intraperitoneal administration²
    - MST = 4.4 months
  - With Gemcitabine → MST 6 months
  - Stage II dogs → 3.4 months
  - Stage II dogs → 4 months

Splenic HSA – Treatment Options

- Splenectomy + injectable chemotherapy (cont.)
  - Adriamycin + cyclophosphamide
    - MST 5 months²
  - VAC (Vincristine, Adriamycin, cyclophosphamide)
    - MST 6 months¹
  - Stage III dz?³
    - ORR (CR + PR) → 86%
    - MST 6.5 months (included SQ HSA; when evaluating all splenic cases MST 4.7 months)
    - CR → MST 8 months
    - PR → MST 4.6 months
    - SD → MST 3.5 months

Splenic HSA – Treatment Options

- Splenectomy + immunotherapy +/- injectable chemotherapy
  - Mixed bacterial vaccine → MST 3m (4m with chemo)³
  - L-MTP-PE + Adriamycin/cyclophosphamide → MST 9 months²

Splenic HSA – Treatment Options

- Splenectomy alone
  - MST 2-3 months (6.25% alive at 1 year)¹
- Splenectomy + injectable chemotherapy
  - Adriamycin alone
    - Q3 week protocol → MST 6 months²
    - Stage II dogs → 2 months
  - Q2 week protocol (dose intensified)³
    - Stage I dogs → 6 months
    - Stage II dogs → 3 months
  - With Gemcitabine → MST 8 months
    - Stage II dogs → 5 months
  - Pegylated liposomal encapsulated Adriamycin
    - No improved survival compared to free Adriamycin³
  - Intraperitoneal administration²
    - MST = 4.4 months
  - With Gemcitabine → MST 6 months
  - Stage II dogs → 3.4 months
  - Stage II dogs → 4 months

References:

¹ Thamm et al, VCO 2012
² Hamner et al, JVIM 2007
³ Sorenmo et al, JVIM 2007
⁴ Sorenmo et al, JVIM 1993
⁵ Kim et al, JAVMA 2007
⁶ Payne et al, VCO 2003
⁷ Dervisis, AAHA 2011
⁸ Alvey et al, JVIM 2011
⁹ Teske et al, VCO 2012
¹⁰ Derme et al, VCO 2012
¹¹ Sorenmo et al, JVIM 2007
¹² Brown et al, JAVMA 1985
¹³ Vail et al, Clin Cancer Res 1995
Splenic HSA – Treatment Options

- Splenectomy + metronomic chemotherapy
  - What is metronomic chemotherapy?
    • Low dose CONTINUOUS therapy (different from maximum tolerated dosing)
    • Anti-angiogenic effects
      - Targets tumor vasculature to starve tumors of oxygen and nutrients
      - Immunomodulatory • decreases Tregs to allow immune system to attack cancer cells
    • Options in veterinary medicine
      - Low dose cyclophosphamide (15mg/m2 PO SID)¹
        » Watch for sterile hemorrhagic cystitis!
      - Low dose chlorambucil
      - Low dose CCNU
      - NSAIDs (+/- MMP inhibitors)
      - Tyrosine kinase inhibitors (ie Palladia)

  ¹ Burton et al, JVIM 2011.

Splenic HSA – Treatment Options

- Alternative therapies
  - Splenectomy + I’m Yunnity¹
    • Mushroom (Coriolus versicolor)
    • Active agent = polysaccharopeptide (PSP)
      - Cell cycle arrest and tumor cell death
      - Boosts immune cell proliferation
      - Alleviates chemotherapy symptoms
      - Enhances tumor infiltration by dendritic cells and CD8+ T-cells
    • Patients treated with 100mg/kg/d
      - Prolonged MST compared to lower dose (6.6 months)
      - No side effects, although large number of pills in larger breed dog (400mg pill size)

  ¹ Brown et al, Evidence-based comp and alt med 2012

Splenic HSA – Treatment Options

- Alternative therapies
  - Yunnan Baiyao¹
    • Chinese herbal supplement
    • Utilized for anti-inflammatory, hemostatic, wound healing, and pain relieving properties
    • Used to control bleeding in dogs
    • In vitro study • causes HSA cell death
    • Dosing
      - <15mg = 1 capsule BID
      - 15-30kg = 2 capsules BID
      - >30kg = 2 capsules TID

  ¹ Wirth et al, VCO 2014

Splenic HSA – Treatment Options

- Other splenic tumors – treatment and prognosis
  - Lymphoma
    - High grade
      • Multicentric
      • Hepatosplenic
    - Marginal zone lymphoma • prolonged MST with surgery alone
  - Splenic stromal sarcomas
    - Prognosis depends on mitotic rate
    - Benefits of adjuvant chemotherapy unknown
  - Fibrohistiocytic nodules
    - Prognosis depends on grade
    - Benefits of adjuvant chemotherapy unknown

OTHER SPLENIC TUMORS
QUESTIONS?