Acute Tumor Lysis Syndrome
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THE ONCOLOGY SERVICE
Overview

- What is ATLS?
- Clinical Consequences of ATLS
- Who is most likely at risk?
- Prevention
- Case Study #1
- Case Study #2
- What is L-Spar?
- Presentation of ATLS
- Treatment
- Clinical Trials available at TOS
- References
What is tumor lysis syndrome

- A uncommon but severe oncologic emergency in veterinary medicine that is caused by the release of massive amounts of potassium, phosphate, and nucleic acids into the circulation system.

- Caused by the rapid die off of tumor cells releasing their cellular contents into the blood stream. This can be caused spontaneously or in response to therapy.
Some Clinical Consequences of ATLS

- Hyperkalemia
- Hyperuricemia
- Hyperphosphatemia
- Hypocalemia
- Disseminated intravascular coagulopathy (DIC)
What in turn can this cause?

- These electrolyte and metabolic changes can then lead to clinical toxic effects such as cardiac arrhythmias, emesis, diarrhea, fever, seizures, and death.
Who is most likely at risk to develop ATLS?

- In people this is a very common emergency and is seen in patients with non-Hodgkin’s lymphoma or acute leukemia.
- Not as common in veterinary medicine: canines with lymphoma are at risk.
- Patient is usually presented with heavy tumor burden and/or not feeling well. The tumors are usually large and bulky.
The large and bulky tumors are usually a mitotically active tumor type.

If the tumor is likely going to respond well to chemotherapy then they are at high risk due to the rapid die off of tumor cells.

Patients with underlying kidney disease

Dehydration
Lymphoma Cytology
Prevention of ATLS

Identify Tumor burden/Risk Assessment

- Presentation with heavy tumor burden such as enlarged lymph nodes
- Measure all lymph nodes at initial visit
- Naïve Lymphoma not started on any therapy such as a CHOP based protocol or steroid use
- How much metastatic disease is noted on diagnostics such as abdominal ultrasounds and chest radiographs.
- Hydration status of the patient
When heavy tumor burden is assessed preventative treatment can be given before starting therapy of choice.

- Start on fluid therapy
- Baseline of blood work and staging recommended prior to starting treatment.
Prevention is the best treatment for ATLS
Tumor burden

Measure all lymph nodes at first visit and follow up with measurements after each treatment to determine response. If at first visit lymph nodes are large and patient is not feeling well then precautions should be taken.
**Case study #1**

Moose was referred to TOS with cytological diagnosis of LSA

- Moose is a 4 ½ year old MN Mastiff
- A physical exam, review of medical records, and an I stat chemistry 8 was performed at consultation.
- Hypercalcemia noted in medical records and on in house istat chemistry
- On ultrasound with primary veterinarian noted diffusely mottled spleen- cytology obtained and still pending
- Generalized lymphadenopathy on physical
- Owner declined other diagnostics such as chest radiographs
- Not on any current medications
History

Chemistry: Ca 13.1 mg/dl

CBC: RBC 8.68, HCT 60.9%, PLT 104,000

Cytology of lymph nodes on 10/30/13 - suspicious of LSA

AUS 11/5/13 - Medial iliac LN prominent, the more caudal LN of the sublumbar chain enlarged and hypo echoic. Spleen mottled and hyper echoic (aspirated)

Cytology of SM LN on 11/5/13: LSA diagnosis

I Stat on 11/7/13: iCa 1.82, HCT 46%, Na, K, Cl within normal limits

Presented to TOS for Oncology Consult on 11/7/13
Physical Exam Findings

- Quiet, alert, responsive
- Dehydrated between 5-8%
- TPR normal
- No murmur or arrhythmia ausculted
- Abdomen soft and non painful-cranial abdominal fullness
- Diffuse edema on right side of the face and right ventral neck
- Facial nodes present but not measured due to patients demeanor
Physical Exam findings continued...

- **Lymph node Measurements**

<table>
<thead>
<tr>
<th>Location</th>
<th>Left</th>
<th>Right</th>
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<tbody>
<tr>
<td>Facial</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Submandibular</td>
<td>7cm</td>
<td>6.8cm</td>
</tr>
<tr>
<td>Prescapular</td>
<td>4.7</td>
<td>5.5cm</td>
</tr>
<tr>
<td>Axillary</td>
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</tr>
<tr>
<td>Inguinal</td>
<td>---</td>
<td>6cm</td>
</tr>
<tr>
<td>Popliteal</td>
<td>4.5cm</td>
<td>4.2cm</td>
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Measure lymph nodes to assess tumor burden
Treatment Plan

Due to the patient presenting with dehydration, lethargy, and heavy tumor burden the plan was for diuresis for several hours, followed with injection of Dexamethasone SP and then L-spar.

We continued with fluid therapy and monitoring overnight post treatment to observe any signs of ATLS.

Moose was discharged after an overnight stay with hospitalization and observation the following day.
Moose was admitted
Administered 2 liters fluid bolus 0.9% saline
Continued on NaCl 500mLs/hr
Dexamethesone SP injection 20mg IV 3 hours post fluids
Changed on P-lyte 220mLs/hr
Elspar injection IM post 4 hours fluid therapy
Sucralfate 2g TID
Famotidine 40mg BID
Overnight fluid therapy continued and monitoring
Chemotherapy treatment

After hospitalization with rehydration now it is time to treat. Wear the appropriate PPE for the type of chemotherapy.
### The Outcome?

**Lymph node measurement 1 week post L-spar and starting steroids:**

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<tr>
<th></th>
<th>Left</th>
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<tbody>
<tr>
<td>SM</td>
<td>both normal</td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Axillary</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Ing.</td>
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<td>---</td>
</tr>
<tr>
<td>Pop.</td>
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</table>
Right sided facial edema resolved
Hypercalcemia resolved
Presented bright, alert, and responsive
The final Outcome?

Careful planning and recognition of tumor burden may have prevented the risk of acute tumor lysis syndrome.

Moose presented the following week with a strong partial response to therapy.
Continued on therapy until noted PD on 6/18/14.
Was euthanized after 8 months after therapy was initiated.
Case study #2
Bayla, a 6-year-old FS Pitbull, was presented to TOS on 6/6/15 for a grade II MCT of the right nostril. The plan was to follow up with surgery for scar revision. Follow up with monitoring was recommended.

Then, Bayla was presented to the Emergency Department as a transfer for pleural effusion and a week-long history of diarrhea on 9/19/15. ER removed 1.7 liters of serosanguinous fluid.
Physical Exam findings

Bayla was transferred to TOS the following Monday 9/21/15 for an initial second consultation

PE findings:
Grade IV/VI heart murmur
Rectal Right sided pedunculated mass with cobble stone texture (not associated with anal sac)

- **Lymph node measurements:**
  - Left
    - SM: 1.5 cm bilobed
    - PS: 2.8 cm
    - Inguinal: 2.5 cm
    - Pop: 1.5 cm
  - Right
    - SM: 2.6 cm bilobed
    - PS: 2.7 cm
    - Inguinal: 2.5 cm
    - Pop: 1.5 cm
Physical exam cont...

- Ultrasound: Spleen abnormal and enlarged and several enlarged intra-abdominal LN
- Chest radiographs: Lymphadenopathy in tracheobronchial LNs and pleural effusion
- In house cytology: Consistent with LSA (Cytology to pathologist pending)
- 9/21/15 Confirmed diagnosis of LSA
Treatment

9/21/15:
- Placed on IVF
- Gave only injection of Dexamethasone SP
- Continue fluid therapy overnight

9/22/15:
- Stopped fluids at noon on 9/22/15 due to increased respiratory rate
- Performed another chest tap: Pulled off 450mLs of fluid
- Gave L-spar injection and another Dexamethasone SP injection
- Discharged on 9/22/15 with GI meds and prednisone taper
The outcome?

- Bayla followed up 1 week after hospitalization/L-spar for continued treatment
- Rectal mass not present
- BAR, normal TPR
- All lymph nodes are normal size except for questionable R submandibular LN slightly enlarged
- Continued on treatment with Vincristine on 9/28/15
- Today Bayla is in a CR and doing great on a CHOP based protocol!
What is L-asparaginase?

- A chemotherapy drug that treats lymphoma
- It is an enzyme
- Healthy cells can produce the essential amino acid asparagine internally
- Cancer cells lack this ability so the cancer cells must pull the asparagine from the blood
So what happens to cancer cells if asparagine was removed from all outside sources?
The cancer cells begin to starve and die off.

L-asparaginase (L-spar) eradicates any asparagine outside of the cells and therefore starves the cancer cells.
How important is hydration when giving chemotherapy

- When optimal hydration is absent the waste products will start to build up due to the slowing of the excretion from the urine.
- As a result electrolyte imbalance will begin to occur.

PREVENTION is the best treatment
Presentation of ATLS

- ATLS usually occurs within hours of initial treatment
- Vomiting
- Diarrhea
- Febrile
- Tachycardia
- Tachypnea
- Hyperphosphatemia
- Hyperkalemia
- Hypocalcemia/hypercalcemia
- BUN and CREAT at first are normal supporting ATLS rather than secondary to acute oliguria or renal failure
Presentation to second day...

- Thrombocytopenia
- Elevated prolonged prothrombin time
- Elevated activated partial prothrombin time

which then leads to diagnosis of.....

DIC
How to Treat if ATLS has occurred
Treatment continued...

- Immediately place intravenous catheter and start IV bolus with 0.9% sodium chloride
- Place on 2x maintenance
- Metoclopramide CRI @ 2mg/kg/day
- Famotidine 0.5mg/kg IV q 12 hr.
- Ondansetron 0.2-0.4mg/kg IV q 8 hr.
You should treat this patient as being in cardiovascular shock.

- Serum electrolytes and blood gases repeated q 4-8 hr.
- Blood pressure q 4 hr.
- Respiratory rate and HR q 1-2 hr.
What to monitor?

CBC and coagulation profile abnormalities = DIC

If clinical for Hypocalcemia start calcium gluconate

If hyperkalemia/bradycardia start insulin and Dextrose

Metabolic acidosis treated with sodium bicarbonate CRI. Sodium bicarbonate (13 mEq/h during first hour and can be reduced to 6.5 mEq/h for additional 4 hours)
Treatment continued...

Start on fresh frozen plasma if DIC is detected.

If elevated aPTT should administer low dose heparin q 8 hr. to prevent thromboembolic event secondary to the DIC.
Human vs dogs developing ATLS

- ATLS is rare in canines as they rarely develop uric acid nephropathy which is the main cause in humans.
- Canines are more likely to develop sepsis as a significant clinical consequence.
Clinical Trials at TOS

3 open clinical trials at our TOS locations.

1. Naïve mammary carcinoma
2. B cell LSA Antibody
3. T cell LSA Antibody

Please contact TOS for any additional information needed or to refer a client.
References

