The Whats, Wheres, and Hows of Treating Companion Animal Cancer

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Stating the obvious

- Animals with cancer usually don’t come to you with a diagnosis or a treatment plan.
- Many times they exhibit no clinical signs whatsoever (ie, just a lump or ADR)
- However, many times they are quite ill upon presentation
- How can we effectively manage this plethora of oncology cases?

Stating the obvious

- Not sick
- Lethargic
- REALLY sick
Stating the obvious

Same tumor with 3 different presentations!

Stating the obvious

Extremely advanced cases

The 3 Questions

• All these different cancers and varied presentations of each cancer-HELP!
• **Question:** How can I figure out how to effectively manage these cases and give the owners all of their treatment options?
• **Answer:** For every case, ask yourself 3 questions
The 3 Questions

• And the 3 questions are (drum roll please):
  – What is it?
  – Where is it?
  – How can I get rid of it?

The 3 Questions

• Question #1: What is it?
  • There are 3 main categories of cancer:
    – Carcinomas-epithelial in origin
    – Sarcomas-mesenchymal in origin
    – Round Cell Tumors-hematologic in origin
  • Why does this matter?
    – Different classes of tumors generally exhibit different biology
    – Different classes of tumors generally exhibit differing metastatic patterns
    – Different classes of tumors respond differently to different treatment modalities

The 3 Questions

• Question #1: What is it?
   – Figuring out what category of cancer an animal has:
     • Fine needle aspirates! I LOVE them—inexpensive, fast results (in-house), minimal risk, and generally quite accurate!
     • FNAs can quickly tell you what category of tumor you are dealing with
     • Look at the slides yourself, and then send them to a commercial lab for comparison
     • FNAs can NOT tell you the Grade of a tumor.
     • Tumor seeding???
The 3 Questions

**Question #1: What is it?**
- Always check a slide to make sure you aspirated enough cells to obtain a diagnosis. If not:
  - Re-aspirate with a larger needle
  - Re-aspirate using suction if you didn’t the first time
  - Be more aggressive—FNAs rarely cause pain, so get ‘er done!

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The 3 Questions

**Question #1: What is it?**
- Adequate cellularity?
  - Only evaluate intact cells
- Do the cells represent the mass?
- Is inflammation present?
  - Inflammation can induce reactive changes consistent with neoplasia
- Smudged cells?
  - No cytoplasm—no good!

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The 3 Questions

**Question #1: What is it?**
- Criteria of malignancy
  - Anisocytosis/anisokaryosis
  - Increased N/C ratio
  - Prominent, multiple, and variable-sized nucleoli
  - Nuclear molding/pleomorphism
  - Course or atypical chromatin pattern
The 3 Questions

• **Question #1: What is it?**
  - Supportive criteria of malignancy
    - High mitotic index
    - Multinucleated giant cells
    - Basophilic cytoplasm

  ![Images of cytological samples]( Images/)

The 3 Questions

• **Question #1: What is it?**
  - FNA results:
    - Round cell tumors-LOVE to give up their cells many times may be an entire slide of cells

  ![Images of cytological samples]( Images/)

The 3 Questions

• **Question #1: What is it?**
  - FNA results:
    - Plasma cell tumors
      - Perinuclear clear zone
      - Multinucleate

    - Histiocytic disease
      - Bizarre cell morphology
      - Erythrophagia

  ![Images of cytological samples]( Images/)
The 3 Questions

• Question #1: What is it?
  – Transmissible venereal tumors (TVT):

  ![Cytoplasmic vacuoles and mitotic figures](image1)

The 3 Questions

<table>
<thead>
<tr>
<th>Lymphosarcoma</th>
<th>Large lymphoblasts</th>
<th>Enlarged lymph nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mast Cell Tumor</td>
<td>Metachromatic granules</td>
<td>Eosinophils; Diff-Quik</td>
</tr>
<tr>
<td>Histiocytic disease</td>
<td>Multinucleate giant cells</td>
<td>Erythro/leukophagia</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>Eccentric nucleus</td>
<td>Prominent Golgi apparatus</td>
</tr>
<tr>
<td>TVT</td>
<td>Ropey chromatin</td>
<td>Location</td>
</tr>
</tbody>
</table>

The 3 Questions

• Question #1: What is it?
  – Histiocytomas:

  ![Histiocytomas](image2)
The 3 Questions

• Question #1: What is it?
  – Carcinomas/adenocarcinomas—epithelial in origin:
    • Will see clustering or clumping of cells on slide

The 3 Questions

• Question #1: What is it?
  – UB TCC

The 3 Questions

• Question #1: What is it?
  – Pulmonary carcinoma:
The 3 Questions

- **Question #1: What is it?**
  - Anal sac adenocarcinomas (neuroendocrine!)
    - Indistinct cell borders
    - Minimal anisokaryosis
    - Grey cytoplasm

The 3 Questions

- **Question #1: What is it?**
  - Squamous cell carcinomas:
    - Robins egg blue, angular cytoplasm
    - Nucleated squamous epithelial cells are NOT normal

The 3 Questions

- **Question #1: What is it?**
  - Sarcomas:
    - Slides TEND to have more blood/fewer nucleated cells

Canine hemangiopericytoma
The 3 Questions

• Question #1: What is it?
  • Osteosarcoma:
    [Images of osteosarcoma cells with very eccentric nuclei]

• Question #1: What is it?
  • A mass may be non-cancerous!
    [Images of lipoma, epidermal cyst, and reactive LN]

• Question #1: What is it?
  • FNA Algorithm:
    Which one would you worry more about?
### The 3 Questions

**Categories of neoplasia:**

<table>
<thead>
<tr>
<th></th>
<th>Cellular Assoc.</th>
<th>Nuclear Location</th>
<th>Cell Shape</th>
<th>Cellularity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carcinoma</strong></td>
<td>Clusters</td>
<td>Central</td>
<td>Round to polygonal</td>
<td>Moderate to high</td>
</tr>
<tr>
<td><strong>Sarcoma</strong></td>
<td>Individual cells</td>
<td>Eccentric</td>
<td>Spindle to stellate</td>
<td>Poor</td>
</tr>
<tr>
<td><strong>RCT</strong></td>
<td>Individual cells</td>
<td>variable round</td>
<td></td>
<td>High</td>
</tr>
</tbody>
</table>

### The 3 Questions

**Question #1: What is it?**
- FNAs are a very good way to identify metastatic LNs:
  - ![Carcinoma](image1.png)
  - ![Mast cells](image2.png)

### The 3 Questions

**Question #1: What is it?**
- Plus-now can send iPhone/Android pics to your friends!
  - ![Lung mass FNAs](image3.png)
The 3 Questions

• **Question #1: What is it?**
  – The “Gold Standard” of diagnosis is a biopsy!
  – Three most dangerous thoughts in Oncology:
    • “Maybe it will go away”
    • “Let’s see if it grows”
    • “Let’s just watch and wait”

![Probable MLD](image)

The 3 Questions

• **Question #1: What is it?**
  – Biopsy methods
    • Needle core biopsy
    • Punch biopsy
    • Tru-cut biopsy
    • Incisional biopsy, i.e., wedge
    • Excisional biopsy
    • Endoscopic biopsy

The 3 Questions

• **Question #1: What is it?**
  – Basic biopsy principles:
    • Careful hemostasis, avoid seromas
    • NO penrose drains!!
    • Proper biopsies do NOT spread cancer cells
    • It’s better to get too much representative tissue than not enough
    • Impression smears can be very helpful!
The 3 Questions

• Question #1: What is it?
  – Submitting a biopsy:
    • Avoid cautery if possible
    • Submit entire sample
    • Use proper fixation:
      – 1:10 of tissue:10% formalin
      – Separate containers for multiple biopsies
      – 1cm or less in thickness to ensure proper fixation
    • Provide appropriate history

The 3 Questions

• Question #1: What is it?
  – What should I pay attention to on the biopsy report when it comes to cancer?:
    • Diagnosis (ie, RCT, carcinoma, sarcoma)?
      – Then:
        • Mitotic index
        • Degree of pleomorphism
        • Vascular/lymphatic invasion
        • Grade of tumor if grade can be assigned
    • You won’t get much of this information unless you tick the microscopic information box on the submission form!

The 3 Questions

• Question #2: Where is it?
  • Staging, staging, staging!
    – Staging is invaluable in determining the tumor burden (extent of disease) that a patient has. In general, the higher the tumor burden, the worse the prognosis.
    – Staging can also be used as a general health check to make sure the patient does not have other cancers or diseases that can affect the overall outcome of your treatment.
      » 23% of dogs with primary brain tumors were found to have a second unrelated neoplasia at necropsy. Most likely related to age at diagnosis.1
    – Of course, staging can cost a fair amount of money


The 3 Questions

• Question #2: Where is it?
  – Staging tests:
    • CBC, serum chemistries, urinalysis
      – Very few malignancies show up in blood
    • Mastocytosis, mast cell disease
    • Thrombocytopenia-hemangiosarcoma
    • Regional LN evaluation imp. for carcinomas, RCT
    • Thoracic radiographs-imp. for sarcomas
    • Abdominal ultrasound
    • Advanced imaging if needed
      – CT scans I love these esp for head tumors
      – MRI we use these mainly for brain tumors
      – Technesium scans

Presented for LF lameness

Techn scan

The 3 Questions

• Question #2: Where is it?
  – Staging information is power!
  – I’m standing on my soapbox:
    • The more information you have and
      the more information you can give to a
      client about their pet’s disease, the
      better you and the client will be able
      to come up with a rational treatment
      plan(s).
  – I’m getting down off of my soapbox.

The 3 Questions

• Question #2: Where is it?
  • In general:
    – Sarcomas spread hematogenously
      » The first capillary bed the tumor emboli usually encounter is
        in the lungs therefore, use thoracic radiographs to document
        systemic spread
    – Carcinomas spread via regional lymphatics
      » FNAs of ipsilateral, and, in some cases, contralateral regional
        LNs is indicated
    – Round cell tumors are considered systemic diseases-they can
      essentially show up anywhere
      » *Mast cell tumors and histiocytic tumors can spread via
        lymphatics
The 3 Questions

• Question #2: Where is it?
  • Remember:
    - There are two types of metastatic disease:
      » Micrometastatic disease: tumor emboli that are present, but they are too small to be detected.
      • Canine osteosarcoma: we know the vast majority of dogs have pulmonary micrometastatic disease at diagnosis; you will not see this on thoracic radiographs, but may see it on a CT scan (but you may not)
    » Macrometastatic disease: obvious tumor emboli that you can see with radiographs, LN FNAs, etc.

The 3 Questions

• Question #2: Where is it?
  • TNM staging scheme is valuable in determining overall prognosis
    - The higher the stage, the worse the prognosis

The 3 Questions

• Question #3: How can I get rid of it?
  • We really only have 3 modalities to treat companion animal cancer:
    - Surgery
    - Irradiation
    - Chemotherapy/Immunotherapy
  • In general, surgery +/- irradiation is used to attain local control while chemotherapy is used to slow or stop the spread/progression of systemic disease.
  • Ask yourself:
    - Am I worried only about local control (ie, a benign tumor)
    - Am I worried only about systemic control (ie, a RCT like LSA)
    - Or am I worried about both (ie, a malignant tumor such as a canine oral melanoma or feline mammary gland tumor)
The 3 Questions

• Question #3: How can I get rid of it?
  – Local control:
    • If you have a patient with a solid tumor that you can see with your eyes, then surgery is the only way to get rid of it!
      – Curative surgery when adequate “clean” margins can be attained
      – Cytoreductive surgery-surgery to reduce the tumor to the microscopic setting-follow with something else?
        » ~50% of canine MCT do not recur even if residual disease is left behind
        » The recurrence rate of canine STS with dirty margins is not 100%
        » Metronomic chemotherapy?

The 3 Questions

• Question #3: How can I get rid of it?
  – Surgical oncology concepts:
    • First chance to cut is the best chance to cure!
      – Cancer is 3-D
      – Muscle and fascia are not sacred
      – Capsule = compressed cancer cells
      – Surgical oncologists like to say, “Go big or go home!”
      – I usually ask the surgeons to take as much normal tissue as possible, while still being able to close the wound.

The 3 Questions

• Question #3: How can I get rid of it?
  – Local control:
    – Always pay attention to histopathologic margins-make sure to mark them in some way and make sure to request margin measurements!
      » What are adequate “clean” margins?
        • For most tumors, my general guidelines are:
          • <5mm-worrisome
          • 5mm-1cm-grey zone
          • >1cm-OK
        » However, some tumors scare me more than others.
          • Feline injection site sarcomas-I like HUGE margins because they have such a high rate of recurrence
          • High grade MCT-same reason
The 3 Questions

• Question #3: How can I get rid of it?
  • Local control:
    – Remember, even benign tumors can lead to significant morbidity and an animal's euthanasia due to a lack of local control
    – Irradiation:
      – Available in most urban areas
      – Definitive irradiation is used to kill residual microscopic disease left by the surgeon, while sparing normal tissue
      – Typically involves 19-23 treatments and costs
        • Start with low-graft STS (biopsies) 5-7 T10-50 or intral with a combination of surgery and irradiation
        • NCSU also offers SRT (stereotactic radiation therapy) high dose administered with precise accuracy to bulk tumors while sparing normal tissues
      – Palliative irradiation is administered to stop or slow down the growth of bulk tumors there are no side effects
        • Usually 1-3 doses which costs ~$2,000-$3,000
        • Very useful to control pain in animals with bone tumors

• Question #3: How can I get rid of it?
  • Systemic control:
    • Chemotherapy
      – Primary modality to treat hematologic malignancies such as lymphomas, leukemias, plasma cell disease, TVTs
      – Can be used either alone or together with surgery and/or irradiation to treat mast cell tumors or soft tissue histiocytic sarcomas
      – Also useful to combat systemic spread of solid tumors
The 3 Questions

• Question #3: How can I get rid of it?
  • Systemic control:
    – Chemotherapy, in any setting, will rarely cure an animal of its disease because:
      » We use ~50% dose reductions used in people to ensure a minimum of GI and BM side effects.
      » We use much less dose intense chemotherapy protocols to ensure less toxicities and a good quality of life during the treatment.
    – Chemotherapy is companion animal has proven efficacy (ie life extension) against many tumor types, such as OSA, HSA, MCT, etc.
    – Chemotherapy has not been definitively shown to extend life in animals with many other types of tumors, such as pulmonary neoplasia, mammary neoplasia, GI tumors, etc.

Feline infection - site sarcomas treated with either surgery on red line or surgery and doxorubicin (blue line)

Canine osteosarcoma treated with amputation alone vs amputation + Carboplatin

Canine MCT treatment algorithm
The 3 Questions

• Question #3: How can I get rid of it?

There are 3 main issues one should consider when formulating a treatment plan(s):

- Costs: Cancer treatment can be extremely expensive
  - You can treat high-grade lymphomas with prednisone only (ie, on the cheap) or with a multi-agent chemotherapy protocol (ie, $7,000-$10,000)
  - Irradiation costs ~$6500
  - BMT costs ~$17,000-$20,000
- Age of animal: Some families are willing to spend more money on a younger animal and not on an animal nearing the end of its natural life
- Owners aggressiveness: Some owners do not believe in giving animals chemotherapy or putting them through an extensive surgery

The challenge is to present a variety of treatment options to the client, based mainly on levels of aggressiveness. Don’t bring right or wrong into the conversation. Let the family decide what they can afford and how aggressive they want to be.

- Therefore, present a variety of options, from least aggressive to most aggressive.
  - Usually, a more aggressive treatment option will be more expensive, but will lead to better overall survival, while having a good quality of life during that time. However, more aggressive treatment options are always more expensive and there is no guarantee that the animal will live longer when compared to no treatment or a less aggressive alternative.
  - “Medicine is not magic” is a phrase I use quite often!
Questions?