

Approaching Advanced Oncology Cases in Difficult Economic Times

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Outline

- Introduction
 - Current state
 - Terminology
- General Economic Case Management Strategies
- Disease Specific Economic Strategies
 - Osteosarcoma
 - Soft Tissue Sarcoma
 - Lymphoma
 - Mast Cell Tumor
- Summary
- Questions ?



Important Terms

- **Standard of Care:** The selected appropriate treatment for a given condition, that is based on scientific evidence and agreed on by specialists in the selected field.
- **Secondary Therapy or Second Line:** An accepted treatment option for a given condition, that has not been found to provide improvement over the standard of care.
- **Definitive Therapy:** Treatment provided with a curative intent.
- **Palliative Therapy:** Treatment provided to alleviate pain or disease associated clinical signs.
- **Conservative Therapy or Supportive Care:** Treatment provided to improve the quality of life for the patient.



Making Good Decisions Early

- **Narrowing the List of Differentials**
 - Look for horses not zebras
- **Reduce Number of Initial Diagnostics**
 - Selecting diagnostics that will provide most information
 - Selecting diagnostics that will alter treatment plan or prognosis
- **Early Conversations with specialists**
 - Provide owner with important information early
 - Discuss goals. Are they achievable?
 - Provide long term prognosis
 - Discuss diagnostics and prioritize!
 - Discuss treatment plan and options



Pretend There Is No Box

- Discuss the standard of care but also secondary care options
 - Compare and contrast the prognosis
- **Ask and listen to owners goals**
 - Determine feasibility of goals
 - Determine possible ways to reach them
- **Read more!**
 - New options, new developments, new strategies
 - Power of the Group!
- Look for clinical trials and research options in your area
 - Fully funded and partially funded options



Reduce Adverse Effects

- **Adverse Effects/Reactions**
 - Chemotherapy or general treatment related side effects can increase treatment cost significantly
 - Hospitalization for neutropenia, vomiting, diarrhea, etc can eliminate the financial ability to continue treatment
 - The impact of adverse effects on the patient can reduce the owners general willingness to treat



Reduce Adverse Effects

- Preventative Steps
 - Pretreatment and post treatment antiemetics
 - Cerenia® (maropitant citrate)
 - Long acting, Q 24 hour dosing
 - Subcutaneous and oral formulation
 - Extremely effective for chemotherapy induced emesis
 - Active and aggressive management of GI issues
 - Probiotics
 - Short course Metronidazole,
 - Diet education
- Reduce Neutropenia Risk
 - Be aggressive when needed
 - Monitor CBCs for trends



Disease Specific Options

- Osteosarcoma (OSA)
- Soft Tissue Sarcoma
- Lymphoma
- Mast Cell Tumor



Osteosarcoma (OSA)

- OSA is defined as "a malignant tumor of the bone" (*osteogenic sarcoma, primary tumor of bone*)
- OSA is the most common primary bone tumor in dogs accounting for up to 85% of skeletal neoplasia¹
- Approximately 75% of OSA occurs in the appendicular skeleton¹



Osteosarcoma (OSA)

•Age of Onset

- Considered to have a bimodal age prevalence
- Commonly seen in middle aged to older dogs, median age of 7-10 years old¹
- There is a large age range with an early peak in incidence at 18-24 months^{1,2}
- OSA has been reported as young as 6 months old^{1,3}



Osteosarcoma (OSA)

•Sex Predilection

- OSA has a slight overrepresentation among male dogs??¹
- Intact male and female patients are reported to be at an increased risk^{1,4}

•Breed/Size

- OSA are most commonly seen in large and giant breed dogs
- Only 5% of OSA occur in dogs weighing <15kg^{1,5}



Osteosarcoma (OSA)

•Primary Site of Predilection

- OSA commonly affect the metaphyseal region of the long bones
- The front limbs are affected two times as often as the rear limbs¹
- Distal radius and proximal humerus are the two most common sites^{1,6}
- Bone adjacent to the elbow is very rarely affected
- Does not cross the joint!



Osteosarcoma (OSA)

•Primary Site of Predilection

- Appendicular OSA of the rear limb is evenly distributed between distal femur, proximal tibia, and distal tibia

- Proximal femur has a slightly lower incidence^{1,6}

- "Away from the elbow, and close to the knee...kinda"
Increased incidence distal tibia



Osteosarcoma (OSA)

•Clinical Presentation

- Patient presents for an acute to chronic onset of lameness and or limb swelling

- Lameness can be weight bearing or non weight bearing, constant or intermittent, +/- localized swelling

- Typically eating, drinking, and otherwise doing well



Osteosarcoma (OSA)

•Initial Evaluation (Look for horses not zebras)

- History of clinical signs

- Onset (acute or chronic)

- Duration

- Appetite, activity, and attitude

- Travel history

- Complete physical exam

- Orthopedic and neurologic evaluation

- Use clinical information to prioritize possible diagnosis

- Afebrile, otherwise healthy patient, with no travel history

- ↓ Likelihood of fungal or bacterial osteomyelitis



Osteosarcoma (OSA)

- Diagnostic Tests (step by step)
 - Limb Radiographs
 - Primary diagnostic step
 - Lateral and craniocaudal views
 - Thoracic Radiographs
 - Right lateral, left lateral, ventrodorsal
 - CBC, Chemistry, Urinalysis



Osteosarcoma (OSA)

- Making a Radiographic Diagnosis vs Pathologic Diagnosis
 - Strong radiographic suspicion can reduce time to treatment and significantly reduce cost to owner
 - Early Oncology consult or Radiology review
- "Aspirates vs Biopsies" When you need a definitive diagnosis
 - Bone fine needle aspiration
 - Decrease trauma to patient
 - Can be done with only mild sedation
 - Cytology provide strong supportive evidence
 - Alkaline phosphatase stain can aid in distinguishing between other sarcomas¹
 - Big savings over surgical biopsy



Osteosarcoma (OSA)

- Radiographic appearance can vary widely
 - Mostly osteolytic to marked bony production
 - Osteoclast vs Osteoblast proliferation
- Key Radiographic Features for a Radiographic Diagnosis
 - Lesion in one of the commonly noted locations
 - Cortical lysis, discontinuity of the cortex
 - New bone production
 - Pallisading reaction, or classic "sun burst" reaction
 - Lifting of the periosteum, new bone production resulting in a triangular appearance "Codman's Triangle"
 - Lesion does not cross the articular cartilage¹



Osteosarcoma (OSA)

•Radiographic Findings Consistent with OSA



OSA of the distal femur:
predominately osteolytic



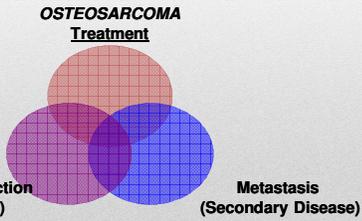
OSA of the distal femur:
predominately osteoproliferative



OSA of the distal radius:
osteolytic and osteoproliferative

Designing a Treatment Plan for OSA

- Definitive OSA treatment ALWAYS involves a 2 fold treatment plan
- Failure to address both aspects results in a significant decrease in prognosis and treatment success



Osteosarcoma (OSA)

•OSA Standard of Care

•Defined as "the treatment option that results in the longest median survival time"

- 1) Surgical resection of the primary tumor
- 2) 3-6 cycles of adjunctive chemotherapy
 - Platinum agent
 - Adriamycin
 - Cell cycle specific drugs

(7,12,13,14,17,18,19,20,21)



Osteosarcoma (OSA)

•Treatment for Local Disease

- Amputation
 - Complete orthopedic and neurologic exam prior to Sx
 - Size and age are not excluding factors
 - Often a quick recovery following surgery
 - Eliminates need for costly long term pain medication
- Palliative radiation therapy
 - Various treatment protocols, and dose fractionation schemes
 - Pain palliation noted in ~74-92% of patients¹
 - Duration of response varies from 2-4 months¹
 - Excellent option in patients with advanced metastatic disease (stage 3), or patients that are not good candidates for amputation

•Bisphosphonates



Osteosarcoma (OSA)

•Treatment for Systemic Disease

- Focused on controlling the development of metastasis
- Adjunctive chemotherapy
 - Carboplatin
 - Cisplatin
 - Adriamycin
 - Carbo/Cisplatin + Adriamycin
 - Carbopatin + Gemcitabine



Osteosarcoma (OSA)

•Treatment for Systemic Disease

- Multi agent protocol vs. Single agent
 - Single agent Carboplatin or Cisplatin adjunctive to surgery¹⁵
 - MST 104-413 days
 - Single agent Adriamycin adjunctive to surgery¹⁵
 - MST 73-257 days
- No significant improvement with combination drug protocols
- Single agent reduces cost and treatment time



Osteosarcoma (OSA)

•Prognosis and MST Summary

- No Treatment
 - Local pain results in a poor quality of life (~2 months)
- Surgery alone
 - MST with surgery alone (in a patient that does not have gross metastatic disease) is ~19 weeks = ~4-6 months ^{7,26}
- Palliative Radiation & adjunctive chemotherapy
 - Results vary, MST~8-10 Months
- Surgery & adjunctive chemotherapy
 - carboplatin and adriamycin combination or as a single agent
 - "standard of care"
 - ~MST= 1 year, 25%=2 years, and 10%=3 years

(7,12,13,14,17,18,19,20,21)



Osteosarcoma (OSA)

•Clinical Trial: Partially Funded!

- Amputation
- Chemotherapy
 - Carboplatin 300 mg/m² IV q 3 weeks x 4
- Randomized to receive
 - Palladia
 - Palladia + metronomic cytoxin



Soft Tissue Sarcoma (STS)

•STS is defined as a heterogeneous group of malignant tumors whose classification is based on similar pathologic appearance and biologic behavior

•STS comprise ~15% of all skin and subcutaneous tumors of the dog

•STS Important Common Features

- Locally invasive
- Appears Pseudocapsulated but has poorly defined histologic margins
- Increased recurrence rate after surgical excision
- Decreased metastatic rate (low to intermediate ~20% high grade ~40%)
- Metastasis is via hematogenous route (lungs most common location)



Soft Tissue Sarcoma (STS)

•Common Soft Tissue Sarcoma Types

- Fibrosarcoma
- Peripheral Nerve Sheath Tumor
- Hemangiopericytoma
- Liposarcoma
- Myxosarcoma
- Leiomyosarcoma
- Rhabdomyosarcoma
- Etc.



Soft Tissue Sarcoma (STS)

•Common Signalment

- Age of onset
 - Commonly seen in middle aged to older dogs, median age 7-10 years old
- Breed/Size
 - There is an increased incidence in large-breed dogs
 - Mixed breed dogs, Rhodesian ridgebacks, and Flat coated retrievers overrepresented



Soft Tissue Sarcoma (STS)

•Clinical Presentation

- Patient presented for the mass itself
- Considered a space occupying disease with clinical signs pending location of primary tumor
- Can have a chronic duration with slow progression



Soft Tissue Sarcoma (STS)

•Diagnostic Tests (How to prioritize)

- Fine needle aspiration vs. biopsy
 - Primary diagnostic step
 - FNA to rule out round cell and some epithelial tumors
 - Benefits of a biopsy
 - Low yield of neoplastic fibroblasts on aspiration
 - Biopsy gains diagnosis and tumor grade

- Thoracic Radiographs (Hematogenous spread)
 - Right lateral, left lateral, ventrodorsal

- CBC, Chemistry (vs. pre-op panel), Urinalysis



Soft Tissue Sarcoma (STS)

•Incisional vs. Excisional Biopsy

- Incisional recommend in most cases
 - Allows for proper diagnosis
 - Provides owner with prognosis prior to definitive therapy
 - Allows for proper treatment planning and options

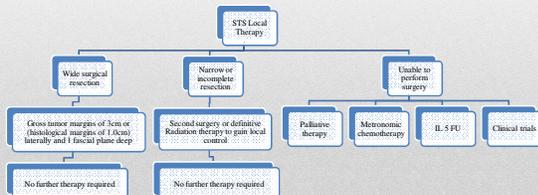
•Excisional biopsy

- Attractive due to one step diagnosis and treatment appeal
- Tumor behavior often results in incomplete resection
- Often increases the need for additional local therapy
- Can increase overall cost to owner



Designing a Treatment Plan for STS

- STS treatment typically focuses on primary tumor control
- Low to Intermediate grade STS treatment success is dependent on local therapy



Soft Tissue Sarcoma (STS)

•Definitive surgery

- Removing the tumor with a complete wide resection
- Gross tumor margins of 3cm laterally
- Histological margins of 1.0cm laterally
- 1 fascial plane deep

•CT performed to determine the overall extent, shape, dimensions, and characteristics of tumors

- aids in proper surgical planning
- Goal is to avoid a second surgery or radiation therapy= \$\$\$



Soft Tissue Sarcoma (STS)

•Palliative Therapy

- Palliative Radiation Therapy
 - Short course therapy 1-6 dose fractions
 - Reduced to no adverse events
 - 75-90% of cases respond
 - Stabilize to reduce tumor size
 - Provide pain control
- Duration of response 2-4 months
 - Can repeat course of therapy
- Reduced cost to owner
 - ~\$800-2500.00
- Slows progression and increases quality of life



Soft Tissue Sarcoma (STS)

•Palliative Therapy

- Metronomic Chemotherapy
 - Low dose daily therapy
 - Goal is anti-angiogenesis
- Novel use of conventional oral chemotherapy agents
 - Cyclophosphamide (cytoxan)
 - Chlorambucil (leukeran)
 - Lomustine (CCNU)
- NSAIDs
 - Piroxicam
 - Rimadyl
 - Previcox
 - Metacam
- TKIs (Growth factor Inhibition)
 - Palladia or Masitinib



Soft Tissue Sarcoma (STS)

•Prognosis and MST Summary

- Reduced metastatic rate ~15-40% pending tumor grade
- Treatment focused on Local control
- No Treatment
 - Local growth results in a poor quality of life (~3-12 months)
- Surgery alone
 - 3cm gross surgical margins (0.5cm histologic) laterally
 - 1 fascial plane
 - Incomplete or narrow surgery increases cost and success
- Definitive RT: curative in 75%
- Palliative Radiation & adjunctive metronomic chemotherapy
 - Results vary, ~4-10 Months
 - Great economic option
 - Improves patient quality of life
 - Slows disease progression



Soft Tissue Sarcoma (STS)

•Prognosis and MST Summary

- Intralesional 5 FU: 6 dogs, DFI=18 months
- Clinical Trials: Fully Funded
- Palliative Radiation & adjunctive metronomic chemotherapy
 - Results vary, ~4-10 Months
 - Great economic option
 - Improves patient quality of life
 - Slows disease progression



Lymphoma (LSA)

•Common Signalment

- Age of onset
 - Commonly seen in middle aged to older dogs, median age of 6-9 years old
- Breed/Size
 - There is an increased incidence in
 - Golden Retrievers
 - Boxers
 - Bull Mastiffs
 - Basset Hounds
 - Bulldogs
 - Saint Bernards
 - Airedales



Lymphoma (LSA)

- One of the most common diagnosed neoplasms in dogs
 - Accounts for 7-24% of all Canine neoplasia
 - 84 per 100,000 dogs 10-11 years old
- 80% of dogs with lymphoma develop the multicentric form
 - Clinical presentation is peripheral lymphadenopathy
- Lymphoma IHC classification (B cell LSA vs. T cell LSA)
 - General population (60-80% B cell vs. 10-33% T cell)
 - Cocker spaniels and Dobies (B cell > T cell)
 - Boxer (B cell < T cell)
 - Golden Retriever (B cell = T cell)



Lymphoma (LSA)

- Due to multicentric presentation systemic treatment is typical
- LSA is considered highly responsive to multiple chemotherapy agents
- Conventional Chemotherapies
 - Induces complete remission (CR) in 60-90% of dogs
 - Median survival time 6-12 months depending on protocol
 - 20-25% of dogs live 2 years or longer
- LSA also has an elevated relapse potential ☹
- Without treatment dogs will die in 4-6 wks



Lymphoma (LSA)

- Lymphoma and Chemotherapy (strategies and achieving goals)
- What determines the Chemo approach?
 - Stage and substage of disease
 - Stage 1- One node
 - Stage 2- Two or more nodes same side of diaphragm
 - Stage 3- Multicentric ≥2 nodes on opposite sides of the diaphragm
 - Stage 4- Splenic or liver involvement, +/- Stage 1-3
 - Stage 5- Extra nodal involvement, Bone marrow OR skin, nasal, CNS, eye, ect.
 - Substage A- Asymptomatic
 - Substage B- Symptomatic
 - Cell Type (B vs T Cell)??
 - Client's comfort with potential side effects
 - Client's financial and time commitment



Lymphoma (LSA)

- Lymphoma and Chemotherapy (strategies and achieving goals)
- Levels of Chemotherapy
 - Induction - First therapy using your standard protocol
 - Reinduction – Second linetherapy using the induction protocol
 - Rescue - Use of drugs attempting to induce remission in cancer that fails to respond to standard therapy



Lymphoma (LSA)

- Induction and Reinduction
 - Multi-Drug protocols demonstrate the greatest MST
 - Most are variations of the "CHOP" protocol
 - C= Cyclophosphamide
 - H= Hydroxydaunorubicin, Doxorubicin, Adriamycin®
 - O= Oncovin®, Vincristine
 - P= Prednisone
 - Other utilized drugs
 - L-Asparaginase, Elspar®
 - Methotrexate, Rheumatrex®, Trexall®
 - Single agent and less aggressive combination protocols
 - Economic and provides an increase MST
 - "COP" protocol
 - Single agent Lomustine with Prednisone
 - Single agent Adriamycin



Lymphoma (LSA)

Protocol	Remission Rate (%)	Median Remission (mo)	Median Survival Time (mo)
U-WM/ CVT X	84-95	8.5 - 10	12-17
COP	70-75	4-6	7.5
DOX.	60-85	4.5-6	6-9
CCNU-P	28-53%	~1-3	3-4 (limited data)

- No treatment results in a 4-6 week MST
- Standard of care is optimal however not the only option
- Economic options are available resulting in significant improvement in MST

Lymphoma (LSA)

•Reinduction/Rescue

- Most dogs will relapse
- Representative of an emergence of tumor clones that develop drug resistant

- Consider effectiveness of previous drug classes
- Customize the protocol to the patient's needs and owner's economic abilities

Protocol	Remission Rate (%)	Median Remission (mo)	Median Survival Time (mo)
Overall	40-80	1.5-2.5	4.8

Lymphoma (LSA)

•Summary

- Lymphoma is a systemic disease and requires systemic treatment

- Standard of care is a multi drug "CHOP" based protocol
- Results in the longest MST

- Other more economic options can provide increased MST
- Discuss a monthly budget with the owner
- Customize a chemotherapy protocol for the individual patient



Mast Cell Tumor (MCT)

•Common Signalment

- Age of onset varies with wide distribution (mean 8.5 yrs)
- No report sex predilection

•Breed/Size

- There is an increased incidence in
 - Boxer
 - Boston Terrier
 - Bulldog
 - Pug
 - Weimeraner

- Labrador retriever
- Beagle
- Schnauzer



Mast Cell Tumor (MCT)

- MCT is the most common cutaneous neoplasms of the dog
 - Represents 7-21%
- Multiple masses are detected in approximately 3-14% of the cases
- Location varies
 - 50-60% found on the trunk
 - 25-45% found on the limbs
 - (cats are more common to have MCT on head and neck)
- Grade is significantly prognostic
 - Grade indicative of metastatic potential
 - Grade 1 <10% met rate vs. Grade 3 ~96%



Mast Cell Tumor (MCT)

- Clinical Presentation
 - Patient presented for the mass itself
 - Patient presented for paraneoplastic symptoms
 - Histamine/ heparin/ proteolytic enzyme release
 - Mass can wax and wane with a history of acute enlargement or reduction in size
 - Can be ulcerated , can feel like a lipoma, can be a plaque...
 - Basically MCT does whatever it wants!



Mast Cell Tumor (MCT)

- Diagnostic Tests (Again step by step)
 - Fine needle aspiration vs. biopsy
 - Primary diagnostic step with mast cell = FNA
 - When in doubt stick it!
 - Pretreat with Benadryl if suspicious of MCT
 - Benefits of a biopsy
 - Biopsy can be used to gain a pre surgery grade in an area not amenable to a 2-3 cm resection
 - Excisional only when 2-3 cm margins are possible
 - Incomplete or narrow excision
 - cost to owner



Mast Cell Tumor (MCT)

•Diagnostic Tests (Continued)

- Thoracic Radiographs (Hematogenous spread)
 - Right lateral, ventrodorsal (2 view)
- Abdominal ultrasound screen
 - Liver and Spleen aspiration
- CBC, Chemistry, Urinalysis
- Bone marrow aspiration
 - For complete staging
 - When there are abnormalities noted on the CBC
- Regional lymph node aspiration
 - Size not an accurate indicator of involvement



Mast Cell Tumor (MCT)

•MCT Treatment

- Surgical excision remains the treatment of choice
 - Traditional 3cm margin of tissue laterally and 1 fascial plane
- Incomplete resection
 - Requires a second surgery or definitive radiation therapy
 - PLAN WISELY!
 - Failing to plan is planning to fail
- When in doubt call us to discuss!



Mast Cell Tumor (MCT)

•MCT Treatment

- Radiation Therapy
 - Definitive RT
 - Highly effective when used for incomplete resection
 - 87 - 93% of patients show no recurrence 5 years post RT
 - Palliative RT
 - Economically viable option
 - Can be used for high stage patients to relieve clinical signs
 - Can be used in conjunction with chemotherapy
 - Patient selection is key



Mast Cell Tumor (MCT)

•MCT Treatment

- Chemotherapy
 - Metastatic MCT/ High grade MCT/ High Risk (location) MCT
 - Adjunctive to surgery/ radiation therapy/ solo therapy
- Conventional Chemotherapy
 - Vinblastine (Velban)
 - Lomustine (CCNU)
 - Prednisone
 - Chlorambucil (Leukeran)
- TKI (Growth factor/ c-kit inhibitors)
 - Palladia™ (toceranib phosphate)
 - Kinavet® (masitinib mesylate)



Mast Cell Tumor (MCT)

•MCT Treatment /Palliative Therapy

- Treatment for the multiple low grade patient
- Step 1-Remove the present tumors if possible
- Step 2-Chemotherapy
 - daily dose therapy (break the cycle)
 - Conventional oral chemotherapy agents
 - Prednisone
 - Chlorambucil (leukeran)
 - TKI (Growth factor/ c-kit inhibitors/ anti-angiogenesis)
 - Palladia™ (toceranib phosphate)
 - Kinavet® (masitinib mesylate)



Mast Cell Tumor (MCT)

•MCT Treatment /Palliative Therapy (cont.)

- Treatment for the end stage patient
 - H1 and H2 inhibition
 - Benadryl and Pepcid are the MCT patient's friend
 - Intralesional steroid therapy
 - Can significantly reduce tumor size
 - Can reduce clinical signs and discomfort
 - Short lived?
 - Risk of tumor necrosis with elevated dose or frequency



Mast Cell Tumor (MCT)

•MCT Summary

- Various presentations and biologic behavior
- Plan treatment course wisely
- Wide surgical excision is the treatment of choice "if possible"

•Combination surgery and radiation therapy results in an excellent outcome

•Advancements in chemotherapy agents has significantly improved our ability to treat all grades and stages of MCT disease

•Palliative options are available in any price range and should be considered



In Closing...

- The economy has stumbled, but we are all still standing.
- One of my favorite quotes sums it up

Success is not final,
Failure is not fatal,
It's the courage to continue
that counts.

Winston Churchill