

Degranulating Mast Cell Tumors

By Pamela D. Jones, DVM, DACVIM (Oncology), DACVR (Radiation Oncology)
Southwest Veterinary Oncology



Figure 1 Interdigital mast cell tumor

It seems the more we learn about mast cell tumors (MCTs), the more complex they become. The increase in complexity is giving us more tools to sort out the good from the bad and leading us to more novel, effective treatment options.

The gross presentation of these tumors varies widely (figure 1) (figures 2 and 3 on pg 2) and diagnosis prior to definitive treatment is the first step and key to early, first-time effective treatment. It is important to keep in mind that while diagnosis can almost always be made by fine needle aspiration cytology (figure 4 on pg 2) excisional biopsy is required for histologic grading of the tumor. This is especially noteworthy as wide surgical excision is the treatment that is most likely to cure the majority of MCTs. Therefore, a definitive diagnosis via cytology allows a curative surgical approach the first time.

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AVS Quarterly Continuing Education Presentation

Wednesday, October 29, 2008

New Directions and Dimensions in Oncology

Dr. Pamela D. Jones, DVM, DACVIM (Oncology), DACVR (Radiation Oncology)

The schedule of the program will be:

6:30 pm: Registration and Dinner, lecture starting at 7:00pm and lasting an hour.

Sponsored by Hills

The course will be held at the Arizona Veterinary Specialty Center, 86 W. Juniper Ave, Gilbert, AZ. (480) 635-1110. This program is approved for 1 Category-1 CE credit by the Arizona Veterinary Medical Association (AzVMA) and attendance is limited to veterinarians. Entry into the building is through the Emergency Animal Clinic. This event is free, and a complimentary catered dinner and lecture notes will be provided. Seating is limited, and reservations will be taken on a first come – first serve basis. To register for the event, please fax the title of the requested event, your name, hospital name, phone, and e-mail address to (480) 892-0540 no later than 48 hours prior to event.

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Degranulating Mast Cell Tumors continued..



Figure 2 Mucocutaneous mast cell tumor



Figure 3 Multiple cutaneous mast cell tumors .

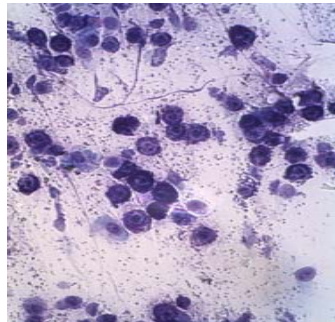


Figure 4 multiple heavily granulated mast cells on cytology.

Staging for MCTs

The second step in treating MCTs is staging. Any MCT has the capability to metastasize therefore staging prior to surgery is essential. Staging for MCTs has evolved markedly in the last decade. Every patient should have a minimum data base of a complete blood count, serum biochemistry profile, and urinalysis. Historically the evaluation of a buffy coat for circulating mast cells was a routine part of staging. Recently, several studies have shown that many other inflammatory diseases including pneumonia, parvovirus, and pancreatitis, as well as patients with neoplasia other than MCTs and post-trauma patients demonstrate mast cells circulating in the peripheral blood.¹ These patients also exhibited a higher mean number of mast cells/buffy coat smear than patients with MCTs. Another study confirmed the presence of mast cells in the buffy coat smears of patients with inflammatory skin diseases.²

Bone Marrow

Bone marrow aspirates also used to be a central part of the staging process. This invasive procedure has fallen out of routine practice. In one study, the incidence of MCT infiltration in MCT patients was as low as 2.8%.³ While the presence of mast cells in the bone marrow is indicative of systemic disease, it is usually easier and more common to find evidence of systemic involvement in other organs such as the liver and spleen.

Evaluating the Liver and Spleen

Abdominal ultrasound is the most sensitive technique for evaluation of the liver and spleen. Generalized infiltration with or without organomegaly is more common than discrete nodules. A fine needle aspirate and subsequent cytology of a structurally normal liver and spleen is generally unrewarding. Further, interpretation of cytology from structurally normal liver and spleen may be compli-

Southwest Veterinary Surgical Service

is now offering

Tibial Tuberosity Advancement (TTA)

in addition to the

Tibial Plateau Leveling Osteotomy (TPLO)

The TTA technique was developed by a team of veterinary surgeons in Switzerland using mechanical principles similar to the TPLO. The goal for both the TTA and TPLO procedures is to alter the mechanics around the stifle to eliminate the cranial tibial thrust generated with weight bearing. The cranial cruciate ligament's weight bearing load is relieved by moving the patellar tendon forward to the point that it is perpendicular to the tibial plateau, allowing the patellar tendon to take over the load. This procedure involves an osteotomy of the tibial crest which is advanced cranially with a spacer between the crest and the main body of the proximal tibia. This spacer is a cage filled with bone graft to hasten healing. A specially designed plate is then applied to further stabilize the tibial crest. TTA offers a unique avenue to simultaneously address cranial cruciate ligament deficiency and patellar luxation. Many factors are considered when determining whether the TPLO, TTA, or another procedure is best for the patient.

“Most importantly histologic grade correlates significantly with survival and has been a valuable predictor of the biologic behavior of MCTs.”

cated by the presence of non-malignant mast cells. Therefore, fine-needle aspiration is indicated only if abnormalities are noted in the liver or spleen.

Lymph Nodes

MCTs commonly metastasize to lymph nodes and therefore all regional lymph nodes should be assessed. Although a lymph node may palpate normal, it is suggested that all regional lymph nodes be examined with fine needle aspiration and cytology. Recall that normal lymph nodes can contain mast cells, for that reason, unless cy-

tology contains clusters or clumps of mast cells that are indicative of metastasis, often lymph node biopsy is necessary for confirmation. Presence of lymph node metastasis generally carries a poorer prognosis than for those without metastasis.⁴ Abnormal lymph nodes found within the abdominal cavity should be assessed by needle cytology as well. Finally, thoracic radiographs rarely exhibit pulmonary involvement but it is important to evaluate the thorax for lymphadenopathy and pleural effusion.

Prognostic Factors

Several studies have elucidated numerous prognostic factors for MCTs. Most importantly, histologic grade correlates significantly with survival and has been a valuable predictor of the biologic behavior of MCTs.⁵ As mentioned previously, grade cannot be determined by cytology, as histologic grade is determined by characteristics of the neoplastic mast cells, number of mitotic figures/10 high power fields, and the extent of tumor invasion into the underlying tissues.

It appears that

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Arizona Veterinary Internal Medicine, PLLC

welcomes

Melissa Riensche

We are pleased to announce that Dr. Melissa Riensche has joined the staff of Arizona Veterinary Internal Medicine. Dr. Riensche is now available for internal medicine referrals on a full-time basis at the Arizona Veterinary Specialty Center.

Dr. Melissa Riensche received her Doctor of Veterinary Medicine degree from Iowa State University in 2004. After graduation Dr. Riensche completed a one-year rotating internship at VCA Animal Referral and Emergency Center of Arizona followed by a residency in internal medicine at the University of Illinois in Champaign-Urbana. Following her residency, Dr. Riensche relocated to Phoenix to join the staff of Arizona Veterinary Internal Medicine. Within the field of internal medicine, she has particular interests in nephrology, gastroenterology, infectious disease, respiratory medicine, and endocrine diseases. Dr. Riensche is board-certified with the American College of Veterinary Internal Medicine.

Arizona Veterinary Specialists

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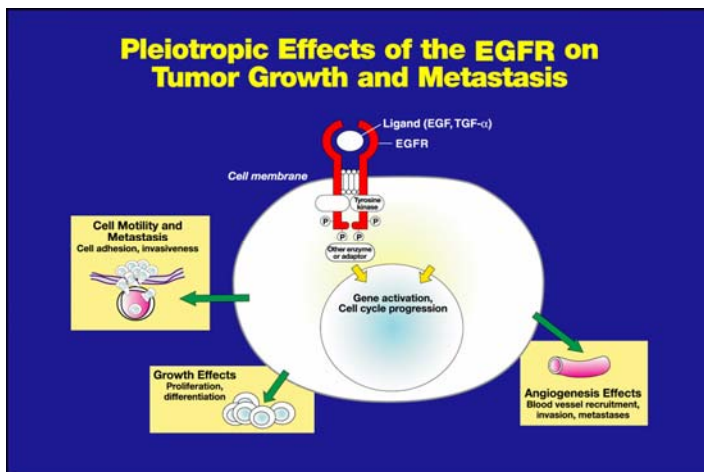


Figure 5 Tyrosine kinase signal transduction

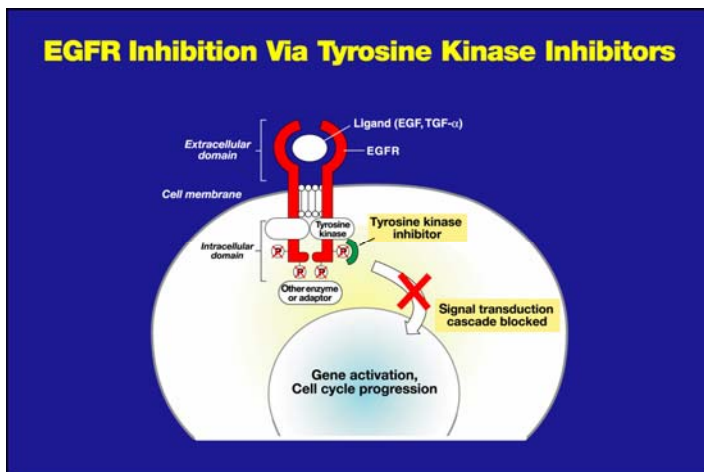


Figure 6 Tyrosine kinase inhibitor blockage of the signal transduction pathway.

more and more MCTs are being classified as grade 2 creating wide variation in the biologic behavior within this group. Fortunately, several proliferative indices are aiding in sorting this group so that we can better predict MCT behavior. These include Ki-67 value, argyrophilic nucleolar organizing regions (AgNOR value), proliferating cell nuclear antigen (PCNA count), and KIT expression pattern. AgNOR value and Ki-67 have been predictive of survival.^{6, 7} AgNOR value, PCNA count, and pattern of KIT expression have all been associated with rate of metastasis.^{8, 9} A comprehensive immunohistochemical panel containing all of these is available through the Flaherty Comparative Oncology Laboratory at Animal Medical Center in New York.

Treatment

Traditionally, treatment of MCTs has consisted of surgical excision. Incompletely excised MCTs are adequately treated with follow up radiation therapy providing >90% 3-year control rate for grade 1 and 2 tumors.^{10, 11, 12} Adjunc-

tive therapies such as corticosteroids and chemotherapy (vinblastine and lomustine) have demonstrated effectiveness against high grade, metastatic, and incompletely excised MCTs.^{13, 14, 15}

Tyrosine Kinase

Kit is a tyrosine kinase receptor on mast cells. Mutations in Kit lead to signal transduction that results in loss of normal cellular growth control (figure 5).¹⁶ Recently, novel small molecular drugs that target Kit have proven activity in clinical studies. These small molecule inhibitors of Kit are administered orally and block Kit phosphorylation and signal transduction that leads to cellular differentiation, survival and function. (figure 6). Response rates as high as 55% were seen in one such study.¹⁶

Although not yet available, Kinavet, a novel tyrosine kinase inhibitor (TKI) is currently being marketed by a European based pharmaceutical company called AB Science. Kinavet blocks the signal transduction through Kit causing

continued on page 5...

"Kinavet blocks the signal transduction through Kit causing cell cycle arrest and apoptosis of mast cells."

cell cycle arrest and apoptosis of mast cells. Patients receiving Kinavet demonstrated a significantly longer time to tumor progression than patients receiving placebo. Pfizer will also have its own TKI product commercially available in 2009.

Ancillary Therapy

Ancillary therapy to protect the patient from the systemic side effects of mast cell degranulation is recommended in all patients with macroscopic disease. Histamine release can be blocked by oral administration of a combination of the H₁ blocker diphenhydramine and one of the H₂ blockers cimetidine or ranitidine.

Summary

MCTs have certainly undergone a dramatic evolution in veterinary medicine. This is one of the reasons why researchers, pathologists, and veterinary oncologists continue to examine MCTs in their complexity. Much like many of the different tumors that plague our patients, their complexity makes them more confusing, but we seem to be gaining some encouraging ground in our understanding and treatment of this multifaceted tumor.

Scientific references available on request.

Meet our Author



Pamela D. Jones, DVM

DACVIM (Medical Oncology)

DACVR (Radiation Oncology)

DR. PAMELA JONES was raised in Tucson and completed her undergraduate studies with honors at Northern Arizona University in 1990. She graduated with honors in 1998 from Colorado State University College of Veterinary Medicine. Dr. Jones went on to the University of Illinois for a three-year oncology residency and became board certified in medical oncology in 2002. She continued her education at Arizona Veterinary Specialists and Southwest Veterinary Oncology with a two-year residency in radiation oncology and became board-certified in radiation oncology in 2004.

You may reach Dr. Jones at

480-635-1110

ext. 2 in our Gilbert office.



Southwest Veterinary Oncology

would like to congratulate

Lynda Beaver, DVM

on the completion of her medical oncology residency and successfully passing the required examinations. Dr. Beaver will continue to see patients at Arizona Veterinary Specialists while advancing through the final phase of the board certification process within the American College of Veterinary Internal Medicine.

Services Offered at Arizona Veterinary Specialists

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- Periodontics
- Dental digital radiography
- Endodontics
- Nasal disease treatment
- Oral disease treatment
- Oral surgery
- Orthodontics
- Restoration
- CO₂ laser for thermoablation gingivoplasty

Oncology

- Linear accelerator radiation therapy
- Chemotherapy
- Immunotherapy
- I-131 radioactive iodine treatment
- Cryotherapy
- Oncologic surgery
- Clinical trials

Ophthalmology

- Biomicroscopy
- Indirect ophthalmoscopy
- Electroretinography
- Ultrasonography
- Applanation tonometry
- Fluorescein angiography
- Glaucoma treatment
- Cataract surgery
- Corneal reconstructive surgery
- Treatment of eyelid abnormalities

Dermatology

- Allergy testing (skin testing) and immunotherapy
- CO₂ laser for ablation of skin tumors
- Video otoscopy
- Testing for food allergies and hypoallergenic diets
- Ear disease diagnosis and treatment
- Bacterial and fungal skin disease diagnosis and treatment
- Cytological smears and microbiologic examinations



- Ectoparasite identification and treatment
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- Special contrast studies
- MRI interpretation
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 - ◆ Bone Scans
 - ◆ Thyroid Scans
 - ◆ Portocaval Shunts

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- Pericardiocentesis
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 - ◆ Gastroduodenoscopy
 - ◆ PEG tube placement
 - ◆ Rhinoscopy
- Endocrine disorders
- Emergency exams
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- Gastrointestinal diseases
- Genitourinary disorders
- Hepatic diseases
- Infectious diseases
- Intensive care treatment
- Immune-mediated diseases
- Nutrition consultations
- Oxygen therapy and critical care
- Pancreatic diseases
- Pulmonary diseases
- Renal disease
- Respiratory diseases
- Second opinion examinations
- Ultrasonography
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- Development of all anesthetic protocols for surgical patients
- Extensive anesthesia monitoring
 - ◆ Blood pressure, both direct and indirect
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 - ◆ Capnography
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 - ◆ Epidural analgesia
 - ◆ Regional nerve blocks

- ◆ Continuous-release analgesics through intravenous infusion and/or transdermal pain patches
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- Chronic pain management consultations



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- Tibial Plateau Leveling Osteotomy (TPLO)
- Triple Pelvic Osteotomy (TPO)
- Total Hip Replacement (THR) both cemented and cementless procedures available
- Tracheal Stenting
- Tibial Tuberosity Advancement (TTA)



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To enhance the quality of our patients' lives, to strengthen the human-animal bond, and to provide a safe and stimulating work environment for all of our team members.

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INNOVATION

We will strive to discover and share knowledge that will continuously improve the veterinary profession.

EXCELLENCE

At Arizona Veterinary Specialists, our standard is excellence in all that we do and the way in which we do it.

COMPASSION

The spirit of all our relationships will be driven by compassion.

PATIENT CARE

We are committed to providing compassionate, ethical, and quality care to our patients. We treat them as if they are members of our own families.

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We will conduct ourselves in a manner that will instill confidence and trust in all of our interactions.

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Check our website for a photo tour of our facility

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