General Information
Mast cell tumors (MCTs) are the most common tumor in the dog and the second most common tumor in the cat. MCTs are primarily a disease of older dogs and cats; however, extremely young dogs and cats have been reported to have MCTs. Canine breeds reported to be at increased risk for MCTs are boxers, Boston terriers, Labrador retrievers, terriers, and beagles. The only feline breed that has been reported to be at increased risk for MCTs is Siamese. Most reports show no significant gender predilection for MCTs in dogs or cats. The etiology of MCTs is presently unknown. Many have suspected a viral etiology due to MCT transplantability to susceptible laboratory dogs (extremely young or immunocompromised) with tumor cells and cell-free extracts. Recent evidence shows that a significant percentage of dogs with higher-grade MCTs have genetic mutations in c-kit (stem cell factor receptor), which may be responsible for the genesis and/or progression of MCTs in dogs. Not all dogs with MCTs have c-kit mutations, suggesting that they are not the only mechanisms for the development and/or progression of MCTs.

Eighty-five to 90 percent of dogs and cats with MCTs have solitary lesions. It is important to note that not all dogs or cats with multiple MCTs have metastatic or systemic mastocytosis. Studies suggest that well-differentiated MCTs are slow-growing, usually < 3–4 cm in diameter, without ulceration of overlying skin, variably alopecic, and commonly present for more than 6 months. In contrast, poorly differentiated MCTs are rapidly growing, variably sized (but generally large), with ulceration of the underlying skin and inflammation/edema of surrounding tissues, and rarely present for more than 2–3 months before presentation. Since most MCTs are of moderate differentiation, signs may be somewhere between these two extremes.

History and Clinical Signs
The history and clinical signs of dogs and cats with MCTs can be extremely variable. Most do not show any clinical signs referable to their MCT; however, some may have signs referable to the release of heparin, histamine, and/or other vasoactive amines. Mechanical manipulation or extreme changes in temperature can lead to degranulation of MCTs and subsequent erythema/wheal formation (Darier’s sign) and gastrointestinal ulceration (anorexia, vomiting, melena, etc.).

Diagnosis and Staging
Fine needle aspiration and cytology (FNAC) are the mainstay for diagnosis of MCT prior to surgical removal. Mast cells of MCTs have a characteristic discrete cell cytological appearance with eccentrically placed nuclei and abundant red to purple (i.e., metachromatic) cytoplasmic granules. Occasional MCTs, predominately undifferentiated MCTs, do not have the classic metachromatic cytoplasmic granules and must be diagnosed via other means (histopathology, special stains, etc.). Once a diagnosis is obtained, staging (looking for disease elsewhere) is routinely recommended; however, the completeness of staging is presently extremely controversial. After an FNAC diagnosis of MCT has been made, this author recommends routine staging diagnostics (full physical examination, bloodwork/urinalysis, FNAC of any local lymph nodes, and abdominal ultrasound). Additional diagnostics such as thoracic radiography and bone marrow aspiration/cytology may be employed.

The use of buffy coat cytology and liver/spleen FNAC is presently controversial in the routine staging of dogs with MCT and this author does not routinely employ these diagnostics for staging of MCTs in dogs. Some oncologists have begun to either not routinely utilize bone marrow aspiration and cytology (BMAC) for MCT staging, or have begun to utilize results of CBC/plt to delineate whether or not to perform a BMAC. This is incredibly controversial and results of a recent publication concerning incidence and risk factors of bone marrow infiltration for canine MCT will be presented at the lecture.

Treatment
Once the diagnosis of MCT has been made with FNAC and/or incisional biopsy and staging has been completed showing no evidence of metastasis to other sites, surgical excision is the preferred choice of therapy. The standard recommendation for complete surgical removal of MCTs has been 3 cm lateral and 1 fascial plane deep to the MCT. The derivation of this recommendation is unknown. This author still recommends continuing use of 3 cm lateral margins and 1 fascial plane deep margins whenever possible, but we published studies that show that 2 cm lateral...
and 1 fascial plane deep margins are sufficient for most grade II MCTs. At present, Seguin et al. (2001) have the best information even though the follow-up time was relatively short (median of only 540 days). Those investigators found a 5 percent recurrence rate in the face of clean margins, an 11 percent second primary tumor development rate, and a 5 percent metastatic rate.

Recent studies in cats with skin/SQ MCT suggest that the vast majority are minimally invasive tumors with low recurrence rates, suggesting that as wide and deep surgical margins may not be as necessary in cats as in dogs. It can not be overemphasized as discussed above that cats with dermal MCT should be staged to ensure they do not have a splenic primary MCT that is metastasizing to dermal and/or other sites.

Dogs and cats with incomplete surgical removal of their MCT should undergo re-resection whenever possible. When re-resection is not feasible, external beam radiation therapy has been found to be an excellent postoperative therapeutic modality affording 75–85 percent control at 4–5 years in dogs with incompletely resected grade II MCT. Recurrence rates for completely resected grade II MCT hover in the 5–20 percent range in the veterinary oncology literature. Recurrence rates for incompletely resected MCTs hover in the 25–40 percent range. At present, we have to recommend additional local therapy for all incompletely resected MCTs in the face of such low-moderate recurrence rates, and additional recent studies will be discussed at the lecture that may help better predict which cases truly need additional local therapy.

The results of a study utilizing radiation therapy for incompletely resected grade III MCT in dogs have been published by Hahn et al. (2004) from Gulf Coast Veterinary Specialists. Thirty-one dogs received 52 Gy of external beam radiation in 18 fractions on a M-W-F basis to the surgical site and draining lymph nodes with no additional therapy (i.e., no chemotherapy). These investigators found a median survival time of ~28 months (range 3–52 months). Only one dog went on to develop systemic MCT metastasis. The results of this trial are controversial within the veterinary oncology community as previous metastatic rates for grade III MCT have been reported to be 55–96 percent. At this time, most oncologists are continuing to use chemotherapy in the treatment of grade III MCT; however, results of this study suggest that the more aggressive use of radiation therapy may be beneficial for grade III MCT.

As discussed above, surgery and radiation therapy should be considered the mainstays of therapy for MCTs. Chemotherapy is a very distant third modality that may be useful for dogs and cats with systemic or metastatic mast cell tumors. Recent studies suggest that CCNU (lomustine), vinblastine, possibly cyclophosphamide, and finally prednisone have limited activity against MCT. The results of studies utilizing chemotherapy will be presented in detail at the lecture.

**Prognosis**

Histopathologic examination of MCTs has been found to be an important prognostic indicator by multiple groups. The Patnaik grading scheme (well-differentiated = grade I, moderately differentiated = grade II, and poorly differentiated = grade III) has shown that 83 percent, 44 percent, and 6 percent of dogs with grade I, II, and III tumors were alive approximately 4 years after surgery, respectively. This grading scheme has not been found to be of use for cats with MCT. Additional negative prognostic factors include advanced stage, caudal half of body location, high growth rates, aneuploidy, and presence of systemic signs. Newly discovered molecularly based negative prognostic factors include increased AgNOR (silver nucleolar organizing regions) scores, increased PCNA/Ki67 immunohistochemistry (IHC) expression (proliferation markers), increased vascularity and/or mitotic index, increased c-kit IHC expression, and the very new Michigan State Low/High grading system. The use of panels of the aforementioned prognostic factors is strongly recommended due to their significant predictive ability for both the subsequent development of metastasis as well as subsequent development of recurrence.

**References**


Suggested Reading


