MAST CELL TUMORS: TREATMENT

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General Information
Mast cell tumors (MCTs) are the most common tumor in the dog and the second most common tumor in the cat.\textsuperscript{1-5} 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 are 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.

Some 85 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; are variably alopecic; and commonly are present for more than 6 months. In contrast, poorly differentiated MCTs are rapidly growing; are variably sized (but generally large), with ulceration of the underlying skin and inflammation/edema of surrounding tissues; and rarely are present for more than 2–3 months before presentation. Since most MCTs are of moderate differentiation, signs may be somewhere between these extremes.

Treatment
Once the diagnosis of MCT has been made with FNAC and/or incisional biopsy and staging has been completed (see section on diagnosis and staging) 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 centimeters 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; however, we recently published studies showing that 2 cm lateral and 1 fascial plane deep margins are sufficient for most grade II MCTs.\textsuperscript{6,7}

At present, there are 2 papers that represent the best information for rates of recurrence, development of distant metastasis, and development of second or more primary MCT in dogs treated with aggressive surgical extirpation with complete staging,\textsuperscript{8} or incomplete staging.\textsuperscript{9} Those investigators found a 5–11% recurrence rate in the face of clean margins, an 11% second primary tumor development rate, and a 5–22% metastatic rate. This author will therefore share with clients, based on the limitations of both of these studies, that dogs with a completely-resected cutaneous grade II MCT (with clean staging preoperatively) will have a 5–10% chance of recurrence, a 10% chance of developing a second de novo primary MCT elsewhere, and a 10–15% chance of subsequently developing distant metastasis.

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% control at 4–5 years in dogs with incompletely resected grade II MCT.\textsuperscript{10-15} As discussed above, recurrence rates for completely resected grade II MCT hover in the 5–10% range in the veterinary oncology literature, but the more important question is the recurrence rate for incompletely resected grade II MCT. Interestingly, recurrence rates for incompletely resected MCTs hover in the 25–40% range.\textsuperscript{16-19} At present, we unfortunately have to recommend additional local therapy (i.e., re-resection or external beam radiation therapy) for all incompletely resected MCTs in the face of such low to moderate recurrence rates. That said, additional recent studies (outlined in the prognostic factors section), will be discussed at the session 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 has been published by Hahn et al. from Gulf Coast Veterinary Specialists.\textsuperscript{20} 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 1 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%. 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. In addition, the use of external beam RT may be beneficial in dogs with cutaneous MCT that has only metastasized to a locoregional lymph node.21

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 tumor. Recent studies suggest that CCNU (lomustine), vinblastine, possibly cyclophosphamide, and finally prednisone have limited activity against MCT.22–29 The results of studies utilizing chemotherapy will be presented in detail at the session.

References


