Mast Cell Tumours

Sarah Boston, DVM, DVSc, Dipl ACVS, ACVS Founding Fellow of Surgical Oncology

Mast cell tumors (MCTs) are the most common maligant skin tumors in dogs, making up 16-21% of cutaneous tumors. This disease is sometimes called the “great pretender” because the gross appearance of this tumor is variable, in part due to the variable biological behavior of this disease. For this reason, it is extremely important to do a fine needle aspirate and cytology on all skin masses in dogs to determine the diagnosis. This disease can affect any dog breed and any location, but middle-aged to older dogs are predisposed and common breeds include Boxers, bulldogs, Boston terriers Labrador retrievers and Sharpeis. The location of MCTs are as follows: ~50% on the trunk, 40% on the limbs and 10% on the head and neck. Most are dermal, but 5-10% are subcutaneous. MCTs have a wide range of biological behaviors. Approximately 80% of MCTs are low to intermediate grade and therefore will have a relatively benign behavior.

After diagnosis of a MCT, it is important to consider the staging that will be necessary for each patient. In all cases, the draining lymph nodes should be palpated, when external and a FNA and cytology should be performed. If the draining lymph nodes are internal, an abdominal ultrasound may be necessary to examine the regional nodes. The decision whether or not to do an abdominal ultrasound for staging of MCT is clinician and case-dependent. In cases with large masses, recurrent disease or lymph node involvement, an abdominal ultrasound should be performed. Small dermal MCT that are amenable to wide resection can be removed with a wide margin and then staging decisions can be made once the histological grade is available. If an abdominal ultrasound is performed, further controversy exists about whether or not to perform a FNA of the spleen and liver if they are ultrasonographically normal. There is literature that suggests that because metastasis of MCT tends to be infiltrative, rather than nodular, the spleen and liver should be aspirated in all cases. There is also literature that supports the view that only spleen and liver that are abnormal on ultrasound should be aspirated because when the spleen/liver are normal on ultrasound, the diagnosis of metastasis is rare. Although there are only a small number of studies evaluating the utility of thoracic radiographs for staging of MCT, the rate of detecting radiographic lung metastasis is low. Thoracic radiography may be warranted, however, as a method of ensuring that there is not concurrent disease in these patients or evaluating hilar lymph nodes. The evaluation of the buffy coat for mast cells is now considered historical only. Further, bone marrow aspiration is also not routinely done because dogs with bone marrow involvement will have widespread and severe disease before the bone marrow is affected.

Although a lot of prognostic factors have been reported in MCT in dogs, significant factors include histological grade, stage of disease, the presence of a c-kit mutation, location and mitotic index. The Patnaik grading scheme grades dermal MCTs based on the degree of differentiation, invasiveness and the mitotic index. MCTs are classified as grade I, II and III. Grade I and II MCTs have a low risk of metastasis, but still require adequate local control. Grade III MCTs have a higher rate of metastasis and a shorter

survival time. Local therapy alone is not adequate and chemotherapy is indicated in these cases. There is significant variability in grading of MCTs, and interpretations of this grading system can vary between pathologists. It has also led to a large number of grade II MCTS and this makes it difficult to predict the behavior of the majority of MCTs. There is a new system that has been proposed that divides MCTs into high and low grade, it is highly repeatable between pathologists and appears to be predictive of survival. This system may replace the Patnaik grading scheme in the next few years. MCTs are staged to indicate the degree of involvement of distant sites. Multiple mast cell tumors are assigned to stage III. However, this is a misnomer because the recent literature suggests that multiple mast cell tumors are likely de novo tumors, rather than metastatic sites and, when treated appropriately at each site, multiple mast cell tumors will not affect overall survival.

Symptomatic treatment of mast cell tumors includes addressing histamine release by treating with diphenhydramine and famotidine. Determining the recommended local treatment will depend on the stage of disease and the owner's goal. Curative intent may involve a wide or radical excision or a marginal excision followed by radiation therapy. For patients with widespread metastasis, or tumors that are no amenable to surgical excision, palliative therapy may include cytoreductive surgery, palliative radiation and/or systemic therapy.

In general, a wide resection is recommended for mast cell tumors. The exact margin required is not definitively known. A recent paper has suggested that 2cm margins laterally are all that is required for tumors that are grade I or II. However, a subsequent study indicated that when 2cm margins are used for grade II MCTs, 10% of the cases had dirty margins. Because of this, I recommend 3cm lateral margins when possible and one fascial plane deep to the tumor. It has also been suggested that neoadjuvant treatment with corticosteroids may facilitate resection. Corticosteriods will decrease inflammation of the tumor and this may make resection easier, however, the corticosteroids will not have an affect on the tumor cells that are peripheral to the tumor. It is possible that corticosteroid treatment may create a false sense of security and the ability to achieve clean margins. It is the author's opinion that corticosteroid use preoperatively should be reserved for cases where cytoreductive surgery and a marginal resection is the goal of surgical therapy.

MCTs respond well to radiation therapy. In general, radiation is used to treat dirty scars after marginal excision or wide excision with incomplete histological margins. Chemotherapy is indicated for high grade tumors and has been shown to prolong survival time. The standard protocol for MCTs is prednisone and vinblastine. Recently, it was discovered that some MCTs have a specific mutation in the tyrosine kinase cell surface receptor for hematopoietic growth (c-Kit). C-Kit is expressed in normal and malignant mast cells and is important for cell survival, proliferation and differentiation. A c-kit mutation means that the receptor becomes independent of normal growth factors and is upregulated beyond normal cell controls. 30-50% of canine MCTs have c-Kit activating mutations. This correlates with a poorer prognosis. It also is a "druggable" target for tyrosine kinase inhibitors such as toceranib.