MAST CELL TUMORS: DIAGNOSIS & STAGING

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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.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 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.

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.

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.2, 3, 5 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) is the mainstay for diagnosis of MCT prior to surgical removal.6, 7 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 (predominantly 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 and the use of the most appropriate W.H.O.-based staging system is presently extremely controversial.8, 9

At present, the W.H.O.-based staging system has dogs with multiple primary MCT (i.e., stage III) having a worse prognosis than dogs with lymph node metastasis (stage II). The most recent literature examining the prognosis of dogs with multiple primary MCT which stage cleanly (i.e., no evidence of metastatic disease) and which achieve appropriate local tumor control have extremely similar outcomes to dogs with cleanly staged and appropriate local tumor control single MCT.8, 9 This suggests that the present W.H.O.-based staging scheme is in need of modification, whereby dogs with cleanly staging multiple primary MCT should be classified as stage II and dogs with lymph node metastasis should be classified as stage III. It is important to point out that dogs with multiple primary MCT should be aggressively staged to determine if they have any evidence of loco-regional (i.e., lymph node) or distant metastatic disease, as further outlined below.

The use of buffy coat cytology for routine staging of dogs with MCT is not recommended, as dogs with non-MCT disease can have higher numbers of mast cells in their buffy coats, and cytologists are unable to differentiate normal mast cells from neoplastic mast cells.10, 11 The routine use of liver/spleen FNAC in the staging of dogs with MCT is presently controversial. A recent study compared mast cell numbers in FNAs of the liver and spleen of clinically normal unaffected dogs with those of dogs with cutaneous MCT and an ultrasonographically normal appearing liver and spleen.12 No clinically important differences were found between the unaffected and affected dogs; thus, routine
Aspiration of an ultrasonographically normal appearing liver and spleen of dogs with cutaneous MCT does not appear to be a clinically useful staging tool.

Some oncologists have either begun to not routinely utilize bone marrow aspiration and cytology (BMAC) for MCT staging, or begun to utilize results of CBC/plt to delineate whether to perform a BMAC. A recent study, of which this author was the senior author, evaluated a series of 157 dogs presented for MCT in which a CBC and bone marrow aspiration were performed. The incidence of bone marrow infiltration at initial staging was 2.8%, and 4.5% overall. Factors significantly associated with bone marrow infiltration included increased age, leucocytosis, anaemia, neutrophilia, monocytosis, eosinophilia, thrombocytopenia, being purebred, and staging at the time of recurrent or progressive disease. Our study suggests that a bone marrow sample may not be indicated for routine staging but may be indicated for those dogs with MCT either having an abnormal hemogram (neutrophilia, monocytosis, eosinophilia, basophilia, anaemia, and/or thrombocytopenia) or presenting for tumor regrowth, progression, or new occurrence.

Based on the above literature, as well as numerous other papers, this author recommends routine staging diagnostics (full physical examination, bloodwork/urinalysis, FNAC of any local lymph nodes, and abdominal ultrasound), after a cytologic diagnosis of MCT has been made with FNAC. Additional diagnostics such as thoracic radiography, bone marrow aspiration/cytology, and/or liver/splenic FNAC may be employed when indicated as outlined above.

References