

What are mast cell tumors and what are their clinical signs?

Mast cell tumors (MCT) are a very common form of cancer diagnosed in dogs. They most commonly occur in the skin, but can also be found in the spleen, liver, lymph nodes and bone marrow. Mast cells are normal cells in the body that are specialized to create chemicals that respond to inflammation and allergies (very similar to a human's reaction to a bee sting). Often, Mast cell tumors are first noticed when a lump is found on the skin (usually on the trunk of the body) and may wax and wane in size over time. Other signs that you may notice include regional swelling of the skin/tissues around the site of the mast cell tumor, as well as more systemic signs including decreased appetite, vomiting, abdominal pain and diarrhea. Many of the regional and distant side effects encountered are associated with the release of chemicals (histamine, vasoactive substances) from the degranulating mast cells within the tumor.

How are mast cell tumors diagnosed and staged?

In order to obtain an initial diagnosis, cytology, involving fine needle aspirates of the suspected mass can be used. This technique confirms that a mass is a mast cell tumor, however, does not provide much more information. A biopsy is needed to determine further information about the mast cell tumor, including the grade of the tumor as well as other features that help determine the tumor's behavior, the necessary staging tests to consider, preferred treatment options and further prognosis. A biopsy can be obtained via an incisional biopsy (a small portion of the tumor is removed), or with surgical removal of the tumor (therapeutic intent). Mast cell tumors are divided into three grades including:

- Grade 1 MCTs are usually benign in nature and most are cured with surgery alone, even if incompletely excised. The metastatic rate of a Grade 1 MCT is less than 10%.
- Grade 2 MCTs are the intermediate grade and the most common (representing ~80% of MCTs). These tumors have a metastatic rate of ~10-50%, and can either act like a Grade 1 or Grade 3. Further diagnostics are usually recommended for Grade 2 tumors to determine their biological nature, including special stain evaluation and c-kit PCR mutation assay.
- Grade 3 MCTs are the most malignant and aggressive. They have a metastatic rate of greater than 50%. Chemotherapy is almost always recommended for Grade 3 tumors.

In addition to the biopsy, staging is also recommended to determine the extent of disease. Current blood work (CBC/Chemistry Profile) and a urinalysis is recommended to evaluate your pet's overall health status. Radiographs of the chest and abdomen are used to look for any enlarged lymph nodes or organ enlargement. An abdominal ultrasound may be advised if the radiographs are suspicious for disease or if your pet's tumor is high grade. Fine needle aspirates of regional lymph nodes or abnormal abdominal organs may also be performed to look for any further evidence of metastasis. The use of a buffy coat smear is controversial and not frequently employed. If bone marrow infiltration is suspected, a bone marrow aspirate may also be recommended by the oncologist.

How are mast cell tumors treated?

Many mast cell tumors are definitively managed with surgery. For those patients with more aggressive presentations (ie high grade tumors, multiple cutaneous masses, the presence of metastatic disease) as well as for those patients where surgery is not an option, multi-modal therapy is recommended and is associated with the best disease control. Options include:

- **Surgery:** This must be done with wide margins to prevent disease recurrence. A minimum of 3-4 cm

margins laterally and 1 facial plane deep is recommended. Depending on the location, wide surgical margins may not be possible. Even with surgical excision, some tumors will recur even after achieving complete margins. Dogs are at a higher risk of developing new mast cell tumors elsewhere on the body during their lifetime after the development of their first tumor.

- **Radiation Therapy:** Radiation therapy has a relatively high success rate of curing grade 1 and 2 MCTs when following incomplete surgical removal (tumor control at 1 year is 90-95%). Side effects are largely limited to the area that is receiving therapy. Radiation therapy can also be used in the gross disease setting with a palliative intent.
- **Chemotherapy:** For dogs with a high risk for mast cell tumor spread or dogs with established disease at multiple sites, systemic treatment with chemotherapy is recommended. Chemotherapy options for MCTs include CCNU (lomustine), Vinblastine and combination protocols that utilize both chemotherapeutics. Steroids and supportive medications are also typically used concurrent with chemotherapy. These medications have about a 40-50% chance of benefit. Other chemotherapeutics that have been investigated for use in MCTs include L-asparaginase, Leukeran and Hydroxyurea.
- **Receptor Tyrosine Kinase Inhibitors (RTKi):** These agents have been previously demonstrated to be effective as a single agent in trials with MCTs. Both Palladia and Kinavet represent commercially available RTKis available for veterinary use. Response rates of MCTs to these RTKis range from 30-70% with dogs having a higher chance to benefit if a mutation is found associated with the target receptor, c-kit. Combination therapy with Vinblastine and supportive medications has been investigated with good tolerability and potential augmentation of tumor response rate and duration noted. Side effects of these medications include decreased appetite, GI disturbance and lethargy.
- **Palliative Care (Steroids, Anti-Histamines, H2 Blockers):** The goal of these medications is a short-term improvement of quality of life and management of sequelae associated with MCTs. Steroids are commonly used in this disease (orally or intralesionally) and may result in a short-term and variable anti-tumor benefit. Anti-histamines (ie Benadryl) and H2 blockers (ie Pepcid) are common supportive medications used to help mitigate side effects associated with histamine release from mast cells including vomiting, diarrhea, nausea, pruritis and edema.
- **Investigational/Clinical Trial Opportunities:** Investigational options and/or clinical trials may also be considered if available and if patients are eligible for inclusion.

What is the prognosis associated with mast cell tumors?

The prognosis for MCTs is influenced by several factors, including the following:

- **Signalment** – Breed predisposition for more benign MCTs (Boxers, Pit Bulls), potentially more aggressive in Shar Peis.
- **Location** – Anatomic locations associated with poorer prognoses include those MCTs associated with the digit, muzzle, oral/mucocutaneous, perineal area, visceral and prepuce. The ability to completely excise that MCT is also significant.
- **Grade, growth rate and special stains** – The higher the grade and higher the index of cell turnover, the more aggressive the MCT will likely be both locally and systemically. Higher grade MCTs are typically associated with a more rapid tumor history and growth rate versus benign MCTs.
- **Stage** – The presence of regional metastatic disease +/- distant metastatic disease is associated with lower survival times.
- **C-kit mutation status** – The presence of a c-kit mutation indicates a more aggressive MCT phenotype; however, also indicates a more favorable response to RTKi therapy.
- **Local tumor recurrence** – Recurrent lesions are typically associated with a more infiltrative local disease presentation, making surgical excision more difficult. They are associated with a more aggressive metastatic phenotype and significantly shorter survival times.