

Canine Mast Cell Tumors: A Review and What's New

Background and Prognostic Factors

Mast cell tumors (MCT) are the most common cutaneous tumor diagnosed in the dog. The biologic behavior of MCTs is highly variable, with many tumors being benign and curable with surgery, and some being highly locally invasive and metastatic to other parts of the body. Several prognostic factors have been identified that can help predict how a tumor may behave. Some of those are:

Histologic Grade and Mitotic Index

The grade of the tumor and mitotic index (MI) is highly predictive of outcome. Two grading schemes are utilized by pathologists to report grade: the Patnaik 3-tiered system (reported as grade 1, 2, and 3) and the Kiupel 2-tiered system (reported as low or high grade). Most low grade, and grade 1 and 2 cutaneous tumors will be cured with surgery alone. High grade and grade 3 tumors are more likely to recur locally as well as metastasize, and most patients die within one year from their disease. MI alone is also predictive of outcome; tumors with a MI > 5 are associated with a worse outcome.

Anatomic location

Location of the tumor is associated with outcome. Oral, subungual, and other mucous membrane sites are associated with a worse prognosis as these tumors are more often high grade. Tumors located on the prepuce or scrotum are associated with a worse prognosis. MCTs on the ear pinnae are more likely to be high grade. Subcutaneous tumors are associated with a better prognosis.

Breed

MCTs that occur in boxers and other brachycephalic dogs (pugs) are more likely to be low grade and benign in behavior. Shar peis are more likely to develop high grade MCTs.

c-kit mutation

The presence of a mutation in c-kit is associated with worse outcome.

Proliferative Indices

Special stains can be performed on tissue of the tumor to evaluate for several different proliferative indices. Indices that are correlated to outcome and survival are Ki-67 and AgNORs; PCNA can also be evaluated though is not as reliable.

Diagnosis and Staging Tests

MCTs are usually easy to diagnose by fine needle aspirate and cytology. Prior to pursuing treatment options, staging tests can be considered. If draining lymph nodes are palpable, those should be sampled and evaluated for evidence of metastatic spread. When MCTs metastasize they typically go to lymph nodes, then spleen and/or liver. If there is concern for a tumor to be high grade (based on location on the dog, growth rate of the tumor, etc.) then abdominal ultrasound with spleen +/- liver aspirates should be performed prior to therapy. A normal appearing spleen on ultrasound can still have metastatic spread and should be sampled regardless of appearance for high grade tumors or tumors/patients with negative prognostic factors¹. If a tumor is likely to be low grade (small, slow growth rate, not in a high-risk location, boxer/pug), then moving forward with surgical excision first is appropriate and additional tests can be performed post-operatively if the grade of the tumor indicates a need for that.

Treatment Options

Treatment options are largely dependent on the stage of the disease as well as prognostic factors.

Surgery

Surgery is the treatment of choice for tumors that are amenable to surgery. Margins of 1-2 cm are usually sufficient for complete removal and clean margins for low grade MCTs. Even in the absence of clean margins, 70-90% of low grade MCTs will not recur locally and adjuvant therapy is not always indicated^{2,3}.

Chemotherapy

High grade and/or metastatic MCTs will typically progress and be life-limiting for dogs, therefore systemic treatment in the form of chemotherapy is indicated. Local control, if possible, should be achieved for better outcome. However, that is not always possible and measurable/bulky MCTs can still be treated with chemotherapy, and responses are reported. Palladia is a non-traditional chemotherapy (tyrosine kinase receptor inhibitor) that targets c-kit mutation and works through several other signaling pathways. Palladia can be used in the macroscopic setting, as well as in microscopic setting of high-grade tumors that have the c-kit mutation.

Radiation Therapy

RT can be used in microscopic disease or in bulky, measurable disease. For tumors that have incomplete margins, if the tumor is high grade or if there are other factors leading the clinician to believe the tumor is likely to recur locally and a second surgery isn't feasible, a definitive course of RT can be used to treat microscopic disease. For large, inoperable tumors, coarse-fractionated or palliative RT can be used to decrease tumor size. There is risk of massive degranulation when radiating larger, bulky tumors.

Stelfonta (tigilanol tiglate)

Stelfonta is a recently approved intra-tumoral injection treatment for any grade of canine cutaneous MCT, and for subcutaneous MCTs below the elbow and hock. Stelfonta is injected directly into the tumor and causes an acute inflammatory response that leads to necrosis of the tumor. The necrosed area then heals by second intention. Tumors cannot be larger than 10cm³. In cases where surgery is not possible, or in patients who are high anesthetic risks, Stelfonta could be a good alternative to surgery⁴.

References

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- 2 Séguin, B. *et al.* Recurrence rate, clinical outcome, and cellular proliferation indices as prognostic indicators after incomplete surgical excision of cutaneous grade II mast cell tumors: 28 dogs (1994–2002). *Journal of Veterinary Internal Medicine* **20**, doi:10.1892/0891-6640(2006)20[933:Rrcoac]2.0.Co;2 (2006).
- 3 Vincenti, S. & Findji, F. Influence of treatment on the outcome of dogs with incompletely excised grade-2 mast cell tumors. *Schweiz Arch Tierheilkd* **159**, 171-177, doi:10.17236/sat00109 (2017).
- 4 De Ridder, T. R. *et al.* Randomized controlled clinical study evaluating the efficacy and safety of intratumoral treatment of canine mast cell tumors with tigilanol tiglate (EBC-46). *J Vet Intern Med* **35**, 415-429, doi:10.1111/jvim.15806 (2021).