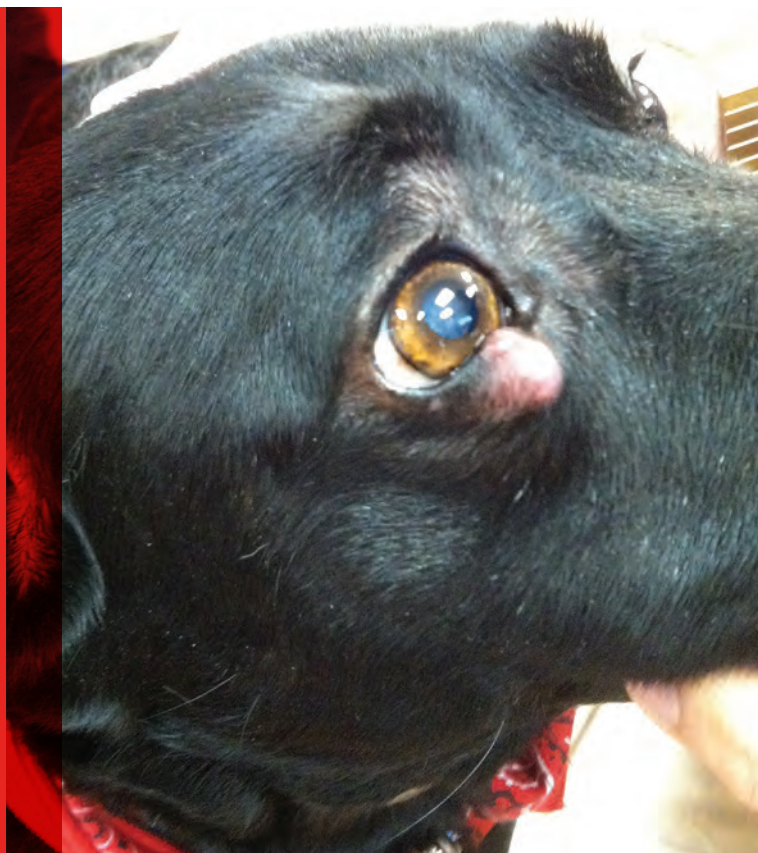


Mast Cell Tumors

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Mast cell tumors (MCTs) are the most common cutaneous tumors in dogs, comprising 16% to 21% of all canine cutaneous tumors,¹⁻⁴ and the second most common cutaneous tumors in cats.⁵

Background & Pathophysiology

The etiology of MCTs in dogs is largely unknown; however, chronic inflammation and alterations in tumor suppressor pathways,^{6,7} as well as altered expression of cell-cycle regulatory proteins⁸ and hormone receptors,⁹ may play a role in the pathogenesis of the disease.

MCTs typically manifest in middle-aged to older dogs (mean, 8-9 years of age). Spay/neuter status does not appear to affect tumor development, and no sex predisposition has been identified.¹⁻⁴ Predisposed breeds include beagles, boxers, golden retrievers, Labrador retrievers, Rhodesian ridgebacks, shar-peis, Stafford-

shire bull terriers, Weimaraners, and brachycephalic breeds.^{1,3,10-12}

The etiology of MCTs in cats is unknown.

History & Clinical Signs

Canine MCTs typically manifest as solitary lesions in the dermis or subcutaneous tissue layers and primarily occur on the trunk or limbs.^{2,13-15} MCTs vary widely in clinical appearance (*Figure 1*, next page). Well-differentiated MCTs are typically solitary, slow-growing lesions that can be present for several months to years and may be mistaken for benign growths (eg, warts, skin tags, lipomas).^{15,16} Poorly differentiated MCTs are commonly ill-defined, rapidly growing, ulcerated, and/or invasive masses.^{15,16} MCTs spread via the lymphatic system to regional lymph nodes, abdominal viscera, and, less commonly, bone marrow; spread of MCTs to the chest cavity (eg, lungs, intrathoracic lymph nodes)

MCT = mast cell tumor

and other body locations is rare.^{10,13,15-17} Although many dogs diagnosed with MCTs do not show demonstrable clinical signs, a subset of dogs can demonstrate tumor-associated signs, including localized tissue reactions (eg, bruising, edema, ulceration, erythema) and/or systemic signs (eg, inappetence, vomiting, diarrhea, fever),¹⁵⁻²¹ secondary to the release of MCT granule substances (eg, histamine, heparin, other vasoactive amines).

Feline MCTs have 3 general presentations: cutaneous, visceral/splenic, and intestinal.^{15,22-29}

Cutaneous MCTs are solitary or multifocal dermal nodules or plaque-like lesions that occur predominantly on the head and neck^{24,25,29-32} and typically affect middle-aged cats; Siamese cats are predisposed.^{24,25,29-31,33} Two distinct histopathologic forms (ie, mastocytic, histiocytic) have been identified; histiocytic forms can spontaneously regress over time, and mastocytic forms may exhibit more aggressive behavior.^{28,29,33-36} Most solitary cutaneous MCTs are behaviorally benign and can be treated via surgical excision alone.^{24,25} Anaplastic or recurrent tumors may require more aggressive



▲ **FIGURE 1** Phenotypic variability of canine MCTs. MCT on the underside of the paw on a pelvic limb in a French bulldog (**A**). Metastatic cervical lymph node cluster in a crossbred dog with a primary MCT on the lateral neck (**B**). Highly vascular and ulcerated MCT near the perineal region of a spaniel (**C**). Ulcerated, recurrent MCT on the lateral thorax of a terrier (**D**)

treatment, similar to canine MCTs.^{24,25} Radiation therapy can be considered in patients with incompletely excised or nonsurgical tumors.³⁴

Visceral/splenic MCTs are sometimes accompanied by cutaneous tumors.^{23,25} Systemic/internal dissemination is common, and most patients are clinically ill at the time of presentation.²³⁻²⁵

Intestinal MCTs are the third most common intestinal tumors in cats.³⁵ Lesions can be focal, infiltrative, or diffuse and predominantly affect the small intestine.^{27,28} Patients are typically clinically ill on presentation. Wide surgical resection is recommended for focal masses.^{27,28}

Diagnosis

Although many canine MCTs can be diagnosed using fine-needle aspiration and cytology, biopsy may be required to provide grading and additional prognostic information. Immunohistochemical stains may be necessary to distinguish poorly differentiated MCTs from other round cell tumors. Staging, including a minimum database (ie, CBC, serum chemistry profile, \pm urinalysis), thoracic and abdominal imaging, and regional lymph node aspiration, should be considered in all dogs with MCTs. Complete staging is important to developing a treatment plan and providing an accurate prognosis in patients with multiple, recurrent (**Figures 1D** and **2**), and/or large MCTs (**Figure 3**) and in dogs with MCTs in locations more likely to trigger aggressive behavior (eg, oral cavity [**Figure 4**]; perineum; subungual, preputial/inguinal regions).^{10,13,15,16} Advanced imaging can help guide treatment planning (eg, surgery, radiation) in patients with large, fixed, and/or invasive tumors. Buffy coat analysis is not informative or specific for the detection of systemic MCTs or in monitoring response to therapy in dogs with MCTs, as the degree of mastocytosis in dogs without mast cell-related illness often exceeds that detected during tumor staging in dogs with MCTs.³⁶

Cats that have multifocal, large, and/or rapidly growing cutaneous tumors, that have palpable



▲ **FIGURE 2** Ill-defined, recurrent periocular MCT in a Labrador retriever crossbreed



▲ **FIGURE 3** 8-cm ulcerated MCT on the caudal thigh of a spaniel



▲ **FIGURE 4** Rapidly growing oral MCT in a pug

MCT = mast cell tumor

organomegaly, and/or that are clinically ill at the time of diagnosis should be staged with a minimum database, thoracic and abdominal imaging, and buffy coat analysis, \pm organ (eg, liver, spleen) aspiration. In cats, buffy coat analysis can provide an index for assessing systemic disease at the time of diagnosis and monitoring response to therapy.³⁷ Mitotic index is the most consistent prognostic factor for cats with cutaneous MCTs.³⁸ There is no well-defined MCT grading scheme for cats.

Treatment & Management

Surgical removal of tumors amenable to wide resection is typically the treatment of choice for cutaneous and subcutaneous canine MCTs. In dogs with large, ulcerated tumors, incisional biopsy can be considered for grading and treatment prior to definitive therapy. Lateral surgical margins of 2 to 3 cm and a fascial plane underlying the tumor are typically recommended when possible.³⁹⁻⁴⁴ Incompletely excised tumors can be treated with scar revision surgery or definitive radiation therapy to address microscopic residual disease. Marginal excision of small, low- to intermediate-grade tumors with margins of 3 to 4 mm may be adequate in preventing local recurrence.⁴⁰⁻⁴⁴ High-grade MCTs have a higher risk for recurrence as compared with low-grade tumors ($\approx 36\%$ vs $\approx 4\%$), regardless of the histologic tumor-free margin.⁴⁴ Nonsurgical and/or recurrent tumors can be treated with palliative radiation.^{45,46} Neoadjuvant radiation can also be used to shrink MCTs prior to surgical removal.

There is no known prevention for mast cell tumors in dogs.

MCT = mast cell tumor

TKI = tyrosine kinase inhibitor

Chemotherapy can be considered for neoadjuvant therapy, postoperatively for incompletely excised tumors in which additional surgery or radiation is not elected or feasible, and for any high-grade or metastatic tumors. Various chemotherapeutic agents have been used alone or in combination in the treatment of MCTs, with overall response rates between $\approx 20\%$ to 90% . The average response rate to chemotherapy in dogs with MCTs is $\approx 40\%$.⁴⁷⁻⁶⁰

For dogs with primary tumors $<3\text{ cm}^3$, electrochemotherapy may be considered if surgery is not elected; a subset of these dogs may experience outcomes comparable with dogs treated surgically.⁶¹⁻⁶³

Novel therapies, including tyrosine kinase inhibitors (TKIs), are available for the treatment of MCTs. Approximately 25% to 30% of canine MCTs have activating mutations in the c-kit gene that can cause unregulated downstream signal transduction that promotes tumorigenesis.⁶⁴⁻⁶⁷ Activating mutations in the c-kit gene have been shown to correlate with increased local tumor recurrence, metastasis, and poorer prognosis.^{68,69} Toceranib phosphate is a veterinary-approved TKI with an overall biologic response rate of 60% and a median time to tumor progression of 4.5 months.⁷⁰ Dogs with an activating mutation in the c-kit gene have increased response rates (up to $\approx 69\%$) to TKI therapy as compared with traditional injectable and oral chemotherapeutics used in the treatment of MCTs.⁶⁹⁻⁷⁴

In general, dogs that have nonmetastatic, low-grade MCTs may experience long-term tumor control or cure with surgery \pm radiation therapy. Patients with several (regardless of grade), non-surgical, recurrent, high-grade, and/or metastatic tumors may benefit from local therapy in combination with chemotherapy or TKI therapy.

Therapies that can help mitigate the effects of MCT degranulation in dogs with bulky tumors include H_1 and H_2 antagonists, proton-pump inhibitors, steroid therapy, and other medications (eg, sucralfate, misoprostol) to treat active or suspected gastric/duodenal ulceration secondary to MCTs.

In cats, a chemotherapeutic standard of care for MCTs has not been definitively established. Positive responses to prednisolone, lomustine, vinblastine, TKIs (eg, imatinib, toceranib), and chlorambucil have been reported.⁷⁵⁻⁸¹ Although cats with the c-kit gene mutation may have an increased chance for response to TKI therapy, the impact of mutation status on overall prognosis does not appear to be significant as compared with dogs.^{75,76,82}

Prognosis & Prevention

The prognosis for canine MCTs is variable. Most dogs with small, low- to intermediate-grade, non-metastatic MCTs can experience long-term (ie, years) survival or, potentially, be cured with surgical treatment alone.^{10,15,16,39,40,45,47-60} Dogs with high-grade, metastatic, or late-stage disease have a guarded to poor long-term prognosis.^{6,10,15,16,18,19,47-60}

There is no known prevention for MCTs in dogs. Early detection and treatment can help ensure a long-term, positive outcome; therefore, it is important to maintain an updated body map of patients and investigate all new nodules and masses, regardless of how innocuous the lesions may appear.

As in dogs, there is no known prevention for MCTs in cats. Most cutaneous MCTs in cats are behaviorally benign, with low rates of local recurrence and metastasis (0%-24%).²⁹⁻³³ In cats with primary splenic MCTs, a median survival rate of 1 to 2 years is possible postoperatively with splenectomy with or without additional therapy.²⁶ Prognosis has historically been considered poor for most cats with intestinal MCTs; however, a recent study reported a median survival rate of \approx 1.5 years in cats treated with combination therapy (ie, surgery, chemotherapy, and corticosteroid therapy).⁸³

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