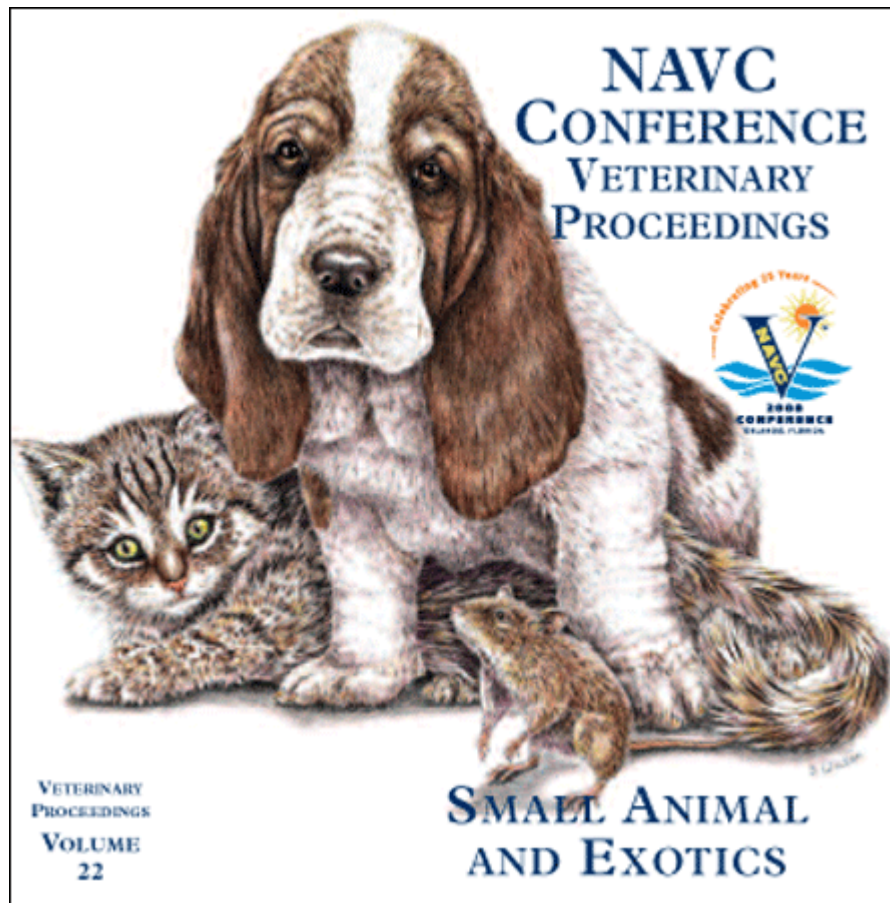


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MAST CELL TUMORS

Nicole Ehrhart, VMD, MS, Diplomate ACVS
Animal Cancer Center
Colorado State University, Fort Collins, CO

CANINE CUTANEOUS MAST CELL TUMORS

Canine cutaneous mast cell tumors (MCT) are a challenge for the veterinarian. Tumors occur in older dogs (mean age 9 years), but any age may be affected. There is no sex predisposition. Flat-nosed English breeds (Boxers, Boston terriers, Bullmastiffs) have a hereditary predisposition. Shar Peis appear to be prone to a particularly aggressive variant. Boxers and possibly golden retrievers tend to have well-differentiated tumors, according to some authors. While the exact etiology of canine mast cell tumors remains unknown, several factors have been implicated over the years. An early study suggested a viral etiology, based on the observation of apparent cell-free transmission of mast cell disease in experimental dogs. No infectious etiologic agent has ever been identified, however. The role of genetic factors and exposure to environmental carcinogens is probable.

Clinical Signs

Most tumors in dogs are solitary, but 10% can present as multiple cutaneous lesions at initial diagnosis. Originally, the presence of multiple concurrent tumors was thought to be a negative prognostic sign, but recently studies have shown that many of these dogs enjoy long-term survival. Most tumors are discovered as a cutaneous or subcutaneous mass with no overt clinical signs. These tumors have a varied appearance and are often mistaken for benign lipomas, skin tags, or cysts. They may be present for many years without changing in size. Alternatively, tumors may degranulate when touched or manipulated, releasing the contents of inflammatory granules. Owners may notice dramatic differences in tumor size over short periods of time due to this swelling and resolving phenomenon after degranulation. Additional paraneoplastic signs associated with release of vasoactive substances are detailed below.

Staging

Staging for mast cell tumors involves grading the local tumor, assessing regional lymph nodes, and distant sites such as liver and spleen. In the dog, 50% of mast cell tumors are benign and cured by surgery. However, an additional 50% are malignant. Malignant mast cell tumors can recur locally or can become metastatic, with the higher histologic grades of tumor associated with more aggressive behavior. Historically, the published literature and text references recommend that mast cell patients be staged with thoracic radiographs, abdominal ultrasound, liver and splenic fine needle aspirates, bone marrow aspiration, and buffy coat analysis. However, in February of 2000, the Veterinary Cancer Society hosted a focus meeting about canine mast cell disease. At this meeting, changes in staging protocols were

recommended. These recommendations were based on the observation that buffy coat blood tests for mast cell leukemia, ultrasound evaluation for liver and spleen involvement, and bone marrow analysis yielded less than 2% positive results in a large series of more than 100 cases. Mast cell tumors that are destined to become metastatic are generally the Grade III tumors, particularly those of axillary and inguinal or preputial location, and the most fruitful site for staging evaluation is the regional node.

Prognostic Factors

Prognostic factors include the location of the primary tumor, in that tumors of the inguinal, axillary, and perineal region may be more aggressive than those arising on the lateral trunk, head or extremities. Histologic grades are associated with outcome; the high-grade tumors are more likely to be metastatic and have shorter overall survival times. In the classic study of cases treated at The Animal Medical Center, 93% of patients with surgically excised Grade I tumors survived 1500 days (approximately 4 years), while 47% of Grade II and 6% of Grade III tumors treated with surgery alone survived for this period of time. Overall, around 50% of all patients in this study were cured by surgery.

Paraneoplastic Disorders

Paraneoplastic disorders caused by MCT include problems associated with degranulation, such as gastroduodenal ulcers from histamine release, coagulopathies from heparin release, and delayed wound healing due to release of proteolytic and vasoactive substances. Management of the paraneoplastic complications of mast cell tumors includes treatment of the primary tumor site, and also symptomatic and direct therapy to counteract the substances released during degranulation. H₂ antagonists such as cimetidine, and the coating agent sucralfate, may be used for dogs with ulcers. Fecal occult blood tests may be helpful in determining subclinical ulcers, but the tests must be performed with care using a meat-free diet before testing to avoid false positives. Protamine sulfate, a heparin antagonist, has been reported to be helpful for prolonged hemorrhage, especially for procedures such as splenectomy. Antihistamine and H₂ antagonists reportedly aid in wound healing.

Treatment

Therapy for mast cell disease is varied depending upon the histologic grade of disease, the clinical stage, and the availability of modalities such as radiation therapy. For the most part, **surgery** is still the mainstay of therapy for local mast cell disease. Surgery with 3-cm margins into normal tissue has been traditionally recommended and is often curative for lower grade lesions. Recently, researchers have questioned the need for such extensive margins, particularly in Grade I disease. The definition of what constitutes a "dirty margin" on histology is also subject to debate. Because mast cells normally reside in dermal tissues, it is

possible that the pathologist may report normal mast cells at the margin of excised tissue. Unfortunately, there is no simple marker that can differentiate malignant from benign resident mast cells. Thus, more conservative surgical excision is being recommended by some authorities. However, in some cases, due to the size and/or location of the lesion, surgery may be incomplete. In these cases, wider surgical margins may be obtained, or radiation therapy for microscopic disease in the tumor bed may be recommended.

Radiation therapy for incomplete margins or for nonresectable disease has a high probability of success in controlling local MCT. In one study of 95 mast cell tumors treated on 85 dogs, 79% were free of tumor at one year and 77% were tumor free at 2 years. Another recent study of dogs that were radiated for incomplete surgical margins showed 96% tumor-free survival at 1 year and 88% tumor-free survival from 2 to 5 years after radiation. Palliative radiation of Grade III mast cell tumors resulted in complete remission with a median duration of 33 weeks or a partial remission with a median duration of 16 weeks (all subject to improvement in quality of life).

Chemotherapy may be reserved for dogs with nonresectable or metastatic lesions. The efficacy of chemotherapy in preventing recurrence or metastasis of mast cell tumor has not been documented. Glucocorticoids are commonly used in treatment of this disease. The combination of vinblastine and prednisone is commonly prescribed for the treatment of mast cell tumors. Intralesional triamcinolone (1 mg/cm of tumor) may also be helpful as palliation in cases where surgical resection is not pursued. CCNU (Lomustine) has been reported to induce responses in dogs with metastatic mast cell disease. However, the response to any of these agents may be unpredictable.

FELINE MAST CELL TUMORS

Mast cell tumors occur in the skin and in visceral sites in the cat. Skin tumors occur in older (mean age 9 years) cats, with no observed sex predilection. Siamese cats are three times more likely than other breeds to develop cutaneous mast cell tumors, which are histiocytic in appearance and prone to spontaneous regression. Visceral mast cell tumors occur in the spleen, mediastinum, and nodes. There is no feline leukemia virus (FeLV) association. Cats also are prone to an aggressive intestinal form of mast cell tumor, which is associated with vomiting, weight loss, diarrhea, and anorexia. Tumors in the intestine are composed of

poorly differentiated cells. Most cutaneous mast cell tumors of cats are well differentiated and benign, but occasionally have been reported to metastasize and often appear as multiple lesions in the skin. Visceral mast cell tumors of the spleen may cause massive splenomegaly and vomiting due to gastrointestinal ulceration from histamine release. When visceral organs such as spleen and liver are involved, mastocytosis and bone marrow involvement may be detected on staging evaluation. Occasionally cats with visceral mast cell tumors will develop multiple metastatic foci in the skin. Mediastinal involvement presents like thymic lymphosarcoma, with dyspnea and pleural effusion. Cytology of the pleural fluid reveals mast cells and eosinophils.

Staging

Staging for mast cell tumors in cats involves a minimum database and buffy coat evaluation for occult mastocytosis, thoracic radiographs, and abdominal ultrasound with fine needle aspiration of involved organs.

Treatment

Treatment of dermal mast cell tumors is surgery, which occasionally must be multiple due to the tendency of cats to have multiple solitary tumors over long periods of time. Because these tumors are well differentiated in general, surgery is curative most often for solitary lesions. Corticosteroids (1 mg/kg/day prednisone) may be helpful. Radiation therapy can be useful for nonresectable or invasive tumors. Visceral mast cell tumors in cats are variable in behavior. Cats may present with massive splenomegaly, prompting the clinician to render a poor prognosis. However, splenectomy alone results in median survival times of 12 months, with some cats reported to live 3 years or more. Treatment of gastric and duodenal ulcers is symptomatic as described for canine mast cell tumors. Intestinal mast cell tumor carries the poorest prognosis of all of these presentations. Intestinal mast cell tumor often is associated with systemic involvement and patients are debilitated from malabsorption before diagnosis. If possible, bowel resection with 5 to 10 cm margins should be performed. Corticosteroids may be palliative for these cats, but most with intestinal involvement die within 4 months of diagnosis. Systemic chemotherapy has been attempted for cats with disseminated MCT. Agents such as used for the dogs may be tried. However, no reports of prolonged survival as a result of chemotherapy have been published.