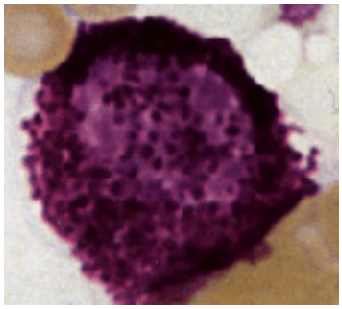
Mast Cell Tumors

What Is a Mast Cell?



Normal mast cell - note the dark purple staining granular structures

A normal mast cell is part of our immunologic defense systems against invading organisms. Mast cells are meant to participate in the war against parasites (as opposed to the war against bacterial or viral invaders). When triggered falsely, they can causes symptoms of allergies. They are bound within tissues that interface with the external world such as the skin, respiratory or intestinal tract. They do not circulate through the body normally. They carry granules of histamine and heparin, which act as "bombs" to fight off parasites and allergens.

And the Mast Cell Tumor?

The mast cell can form a tumor made of many mast cells. When this happens, the cells of the tumor are unstable. This means they release their toxic granules with simple contact or even at random creating allergic symptoms that do not correlate with exposure to any particular antigen.

Mast Cell Tumors in Dogs

Mast cell tumors are especially common in dogs, accounting for approximately one skin tumor in every five. The Boxer is at an especially high risk, as are related breeds, including English Bulldog, and Boston Terrier. Also at higher than average risk are the Shar pei, Labrador Retriever, Golden Retriever, Schnauzer, and Cocker Spaniel. Most mast cell tumors arise in the skin but technically they can arise anywhere that mast cells are found (i.e., anywhere I the body). The mast cell tumor does not have a characteristic appearance though – it can take on many different appearances. Because of the tumor's ability to cause swelling through the release of granules, it is not unusual for the owner to notice a sudden change in the size of the growth or, for that matter, that the growth is itchy or bothersome to the patient. Often, mast cell tumors will seem to grow and shrink in size over time.

Diagnosis can often be made with a needle aspirate, which collects some cells of the tumor with a needle, and the cells are examined under the microscope. The granules have distinct staining characteristics leading to their recognition. An actual tissue biopsy, however, is needed to grade the tumor and grading of the tumor is crucial to determining prognosis.

Grading the Mast Cell Tumor

The pathologist grades mast cell tumors when the biopsy sample is read. The grade is a reflection of the malignant characteristics of the cells under the microscope (which of course generally correlates to the behavior of the tumor) with Grade I being benign, Grade III being malignant, and Grade II having some ability to go either way. The grading system applies only to dogs, not cats.

Grade I Tumors

This is the best type of mast cell tumor to have. While it may tend to be larger and more locally invasive than is outwardly, it tends not to spread beyond its place in the skin. Surgery should be curative, if the entire tumor is removed. If the original biopsy sample shows that the tumor has only narrowly been removed or that the tumor extends to the margins of the sample, a second surgery should promptly be done to get the rest of the tumor if at all possible. If the grade I mast cell tumor is incompletely excised it will likely grow back in time; it is best to get it all and be done with it as quickly as possible.

Grade II Tumors

This type of tumor is somewhat unpredictable in its behavior. About 70% or more of these tumors will not recur if surgically removed completely. If a grade II mast cell tumor recurs, more surgery, and even radiation therapy or chemotherapy can be done. In some case, treatment of recurring grade II mast cell tumors is curative. Recent studies have shown that radiation therapy administered to the site of the tumor can cure greater than 80% of patients with recurring mast cell tumors, as long as the tumor has not already shown distant spread.

If you have a grade II mast cell tumor diagnosed by biopsy report, the sections at tissue at the lab can be sent to Michigan State University Diagnostics Lab for what is called a Prognostic Mast Cell Tumor panel, which can tell us much more about whether the grade II tumor is likely to spread, and whether chemo is indicated. These prognostic panels cost between $200 and $250 to run.

Grade III Tumors

This is the worst type of mast cell tumor to have. Grade III tumors account for approximately 25% of all mast cell tumors and they behave very invasively and aggressively. If only surgical excision is attempted without supplementary chemotherapy, a mean survival time of 18 weeks (4-5 months) can be expected. Adding chemotherapy and/or radiation therapy can increase survival time, though in most cases, grade III mast cell tumors can not be cured.

Staging The Mast Cell Tumor

Because grade I mast cell tumors are benign, they do not need to be staged. Because most grade II mast cell tumors do not recur if completely removed, many debate whether all grade II mast cell tumors should be staged. Most agree that recurring grade II and all grade III mast cell tumors should be staged. In order for a rational therapeutic plan to be devised for a recurring grade II or any grade III mast cell tumor, the extent of tumor spread (or stage of the tumor) must be determined. Using the stage and the grade, a treatment plan can be devised. The tumor is staged 0 through IV as described below:

Stage 0: one tumor but incompletely excised from the skin

Stage I: one tumor confined to the skin with no regional lymph node involvement

Stage II: one tumor confined to the skin but with regional lymph node involvement present

Stage III: many tumors or large deeply infiltrating tumors, with or without lymph node involvement

Stage IV: any tumor with distant spread evident, most often to the liver or spleen. This stage is further divided into substage a (no clinical signs of illness) and substage b (with clinical signs of illness).

Your veterinarian may recommend the following tests:

Basic Blood Work. A basic blood panel is part of this evaluation process and should be obtained at this point if it has not already been obtained. This testing will help show any factors that limit kidney or liver function and thus determine what drugs of chemotherapy can or cannot be used. It also will show if there are circulating mast cells in the blood (a very bad sign) or if anemia (low red blood cell count) is present which might be related to the tumor. Test usually include CBC, general health profile and electrolytes.

Local Lymph Node Aspiration. The lymph nodes local to the site of the tumor should be aspirated (if they can be found) to see if the tumor has spread there. Finding mast cell tumor in the lymph node shows that chemotherapy is indicated.

X-rays and ultrasound with aspiration of the liver and spleen. The size of the spleen and liver can be evaluated with x-rays but ultrasound guidance is generally needed to withdraw some cells from each organ for examination under the microscope, to look for mast cells. The spleen is an organ of the lymph system and the presence of tumor in the deeper lymph organs such as the spleen and abdominal lymph nodes should be assessed. While the mast cell tumor does not spread to lungs the way other tumors do, there are many lymph nodes in the chest and it is helpful to radiograph the chest to assess the size of these lymph nodes and thus help determine the extent of tumor spread.

Buffy Coat Smear. The buffy coat is the small layer of white blood cells that floats atop the layer of red blood cells when a capillary tube of the patient's blood has been centrifuged. This layer of cells can be smeared onto a microscope slide and checked for circulating mast cells. This process was once considered an important method of evaluating mast cell spread in dogs but has more recently been found not very helpful on dogs. This test is still of use for cats.

Bone Marrow Aspirate or Biopsy. This is done usually only of there are low cell counts on the Complete Blood Count (CBC), suggesting that mast cell tumor might be invading the bone marrow and squeezing other cells out. When found in the bone marrow, mast cell tumor can be very difficult to treat.

Other Factors In Prognosis

As if grade and stage do not pose enough food for thought, other factors add in to the prognosis.

Anatomic Location: Mast cell tumors arising in the following areas tend to be the most malignant: nail bed, genital areas, muzzle, and oral cavity. Mast cell tumors that originate in deeper tissues such as the liver or spleen carry a particularly grave prognosis.

Growth Rate Of Tumor: Tumors that have been present for months or years tend to be more benign. Those that appear and get very large quickly are more difficult to treat.

Therapy

Therapy for mast cell tumors consists of surgery, radiation therapy, and chemotherapy (as is the case for almost all types of cancer). What combination of the above is chosen depends on the extent of spread and malignant characteristics of the tumor.

Surgery

If the tumor can be cured with one or even two surgeries, this is ideal. Mast cell tumors can sometimes by highly invasive and very deep and extensive surgical margins (at least 3 cm in all directions) are needed. If for some reason, a grade I or II tumor cannot be completely excised, radiation therapy makes an excellent supplement.

Radiation Therapy

While radiation therapy tends to be expensive, the potential to permanently cure a grade II mast cell tumor is likely worth it. Like surgery, radiation is a therapy most appropriate for localized disease. In other words, it works only on the spot irradiated. If the tumor stages so as to show more distant spread, radiation becomes less helpful and medications (chemotherapy), which can be delivered to the tumor through the patient's blood becomes necessary.

In January 2004, Hahn, King and Carreras published a study where radiation therapy was used to treat incompletely removed Grade III mast cell tumors, showing more promising results than previous treatment protocols. Approximately 65% of dogs achieved remission and 71% were alive one year after treatment.

Chemotherapy

Chemotherapy might sound very scary at first, because it conjures up images of very sick people who are losing their hair. All chemotherapy really means is using drugs to treat disease. Unlike in human oncology, where the patient is pushed as far as possible in an attempt to get a cure, knowing the cost may be worth it, veterinary oncology takes a different approach. The goal of chemotherapy for dogs and cats is to kill cancer cells, without making the pet sick if at all possible, to increase quality and quantity of remaining life. Pet almost never lose a great deal of hair when undergoing chemotherapy.

Currently three anti-cancer drugs have been particularly helpful in combating mast cell disease: Corticosteroids (such as prednisone), Lomustine (CCNU), and Vinblastine.

Corticosteroids seem to be directly toxic to mast cells and can lead to a brief remission even when used alone. They are particularly inexpensive treatments and definitely worth trying should more powerful chemotherapy drugs be considered too expensive or troublesome.

The mast cell tumor releases histamine-containing granules that lead to inflammation and increased stomach acid secretion. These unpleasant symptoms may be alleviated with the use of H1 blockers (antihistamines such as Benadryl® and others) as well as H2 blockers

(antihistamines such as Pepcid AC®, Tagamet®, Zantac® and others).

Vinblastine and CCNU are anticancer drugs which have been shown to be effective for treatment of mast cell tumor. Palladia is a new drug that is reserved for severe grade III mast cell tumors, because side effects can be severe.

Mast Cell Tumors in Cats

The mast cell tumor situation is slightly different for cats although most of the same concepts hold true (so if you skipped the canine section to read the feline information it would be best to go back and read the canine section). Mast cell tumors classically affect older cats; in one study the average age was 10 years. Pathologists divide feline mast cell tumors into two forms: well differentiated and poorly differentiated. The well-differentiated tumor is generally more benign in its behavior while the poorly-differentiated tumor behaves more malignantly. Mast cell tumors in cats are also classified by their location into two forms: cutaneous (located in the skin) and visceral (located internally). An unlucky cat may have both.

Cutaneous (Skin) Forms

The skin form of the feline mast cell tumor often arises around the head and neck, though it can be anywhere. Lesions may be solitary or multiple although multiple lesions do not necessarily mean the situation is worse. However, if there are many mast cell tumors, that would constitute a lot of inflammatory biochemicals and more symptoms for the cat.

Treatment of choice would be surgical excision. If surgical excision is incomplete, radiation therapy as a follow-up is generally successful at cleaning up any leftover cells.

Visceral Form

As you might guess, mast cell tumors located internally are more serious than those in the skin. The most common organs involved are spleen, liver, and intestine. Vomiting, appetite loss, and weight loss are the most common symptoms. As with the cutaneous form, surgery is the treatment of choice for visceral mast cell tumor in cats. However, surgical removal of these masses are often more difficult when visceral. No single chemotherapy protocol has emerged as being particularly more successful than others.

Unlike the canine situation, it is not all that helpful to stage the mast cell disease in cats, as tumor cells in other locations do not alter prognosis for this disease in cats. The most telling piece of information for prognosis in cats actually comes from the history: appetite. Cats that are eating decently at the time they are first brought to the veterinarian have a median survival of 19 months, while cats that are not eating have a median survival of 8 weeks.

Splenic Mast Cell Tumor

Luckily, the spleen can be removed leading to a rapid recovery in many cases. The median survival after splenectomy is 14 months (vs. 4-6 months if the spleen is left in place). This is not to say that the cat is cured with splenectomy, but removing the spleen frees the cat from the bulk of the mast cells quickly and it takes time for the tumor to regrow.

References:

1. VeterinaryPartners.com