

Mast Cell Tumors in the Dog
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Biology and Function of Mast Cells

Mast cells are discrete round cells roughly 1-3x the size of a neutrophil. They possess a round to oval nucleus and distinct cytoplasmic granules that stain with dyes such as toluidine blue, geimsa, and methylene blue. Such staining is due to the affinity of these basic dyes for the acidic proteoglycans contained in the mast cell granules. Some of these dyes assume a different color when bound by the granules than they do when staining nuclear DNA, so that the granules are often called "metachromatic." Although mast cells may be visualized on hematoxylin and eosin stained sections, the dyes described above are utilized to definitively characterize mast cells. Moreover, mast cell granules may not be visualized with stains such as Diff-Quick, precluding identification on some cytologic specimens.

Mast cells are derived from bone marrow precursor cells. They leave the bone marrow in a presumed immature state and migrate to many tissues, particularly those having primary contact with foreign antigens (skin, respiratory and gastrointestinal tracts) where they then mature into tissue mast cells. The local tissue microenvironment in which mast cells mature determines the subsequent functional capacities of these cells.

Matrue mast cells bind IgE on their cell surface through expression of the high affinity IgE receptor (FcERI). Mast cells also express receptors for complement components. (particularly C5a). The primary manner in which mast cells are activated is by crosslinking the FcεRI-bound IgE on their cell surface, leading to the release and production of various mediators.

Including:

- a. Contents of granules such as histamine, heparin, chondroitin sulfate, mast cell proteases, and others.
- b. Lipid mediators such as prostaglandins, leukotrienes and platelet activating factor
- c. Cytokines such as TNFα, IL-3, IL-4, IL-5 and IL-6.

The mediators described above lead to several reactions including increased vascular permeability, vasodilation, smooth muscle spasm, pruritis, anticoagulation, and activation of eosinophils and neutrophils. Collectively these effects can lead to local hypersensitivity reactions, or more seriously, systemic hypersensitivity (anaphylactic shock). As such, mast cells have primarily been associated with allergic reactions/disorders. However, it is now evident that mast cells appear to play an important role in the initiation of innate immune responses, particularly with respect to sustaining neutrophil migration and activation in response to bacteria. Indeed, mast cells are often seen at sites of inflammation, as well as in reactive lymph nodes. Therefore, in addition to playing a role in the induction of pathologic allergic responses, mast cells are critical players in protective immune responses.

Canine Mast Cell Tumors
Incidence and Signalment

The MCT is the most common skin tumor of the dog, and one of the most common malignant tumors noted in the canine population. While MCT's are usually found in older dogs (8-9years), they have also been reported in younger dogs (6-9). Several breeds appear to be at increased risk for the development of MCT including dogs of bulldog descent (boxer, Boston terrier, English bulldog), Labrador and golden retrievers, cocker spaniels, schnauzers and Shar-Pei. No sex predilection has been reported.

Etiology

The etiopathogenesis of MCTs in the dog is unknown, as is the reason for the extremely high incidence in this species. Although some studies have suggested the possibility of a viral cause, there is no epidemiological evidence to indicate horizontal transmission of tumors. As most of the tumors arise in the skin, it has also been suggested that topical carcinogens may play a role in this disease. No reports exist to imply such a cause, and

there appears to be no particular regional distribution of these tumors. The increased incidence of MCTs in certain breeds suggests the possibility of an underlying genetic cause and studies are ongoing to identify these putative genetic risk factors. Interestingly, while dogs of bulldog ancestry are at higher risk for MCT development, it is generally accepted that MCTs in these dogs are more likely to be benign. Additionally, it was recently demonstrated that Pugs develop multiple mast cell tumors that behave in a benign fashion. In contrast, anecdotal evidence suggests that Sharpeis develop MCT's that are biologically aggressive.

Kit is a receptor found on mast cells (as well as hematopoietic stem cells and melanocytes, among others) and Kit signaling is required for the differentiation, survival, and function of mast cells. Mutations in Kit have been demonstrated to occur in systemic mastocytosis in people and these mutations lead to excessive signaling, resulting in loss of growth control. Several authors have recently identified the presence of Kit mutations in dog MCTs and these also resulting in uncontrolled signaling. While up to 30% of all dog MCTs may have Kit mutations, these are not germ-line in nature (are not inherited) and occur during the process of tumor development.

History and Clinical Signs

The overwhelming majority of MCTs in the dog occur in the dermis and subcutaneous tissue. Rarely, primary MCTs may present in other sites such as the oral cavity, nasopharynx, larynx, and gastrointestinal tract. Visceral MCT involving the spleen, liver and/or bone marrow is usually the result of systemic spread of an aggressive primary cutaneous MCT, although it can occur as an independent syndrome. Primary mast cell leukemia in the dog is extremely rare.

Cutaneous MCTs usually occur as solitary nodules, although roughly 10 to 15% of dogs will present with multiple tumors. Approximately 50% of cutaneous MCTs occur on the trunk and perineal region, 40% on the limbs, and 10% on the head and neck. Perhaps most importantly, the clinical appearance of MCTs can vary widely. Dermal MCT may be well circumscribed, raised and firm, or the surface maybe erythematous and ulcerated; invasion into the subcutaneous tissue may be present. MCTs arising in the subcutaneous tissue are often poorly circumscribed and may resemble lipomas. It is therefore not possible to identify a cutaneous lesion as a MCT simply by its appearance. Cutaneous MCTs may also be present for various lengths of time. In general, MCT that are slow growing and present for at least 6 months are more likely to behave in a benign manner, while those that are rapidly growing large tumors are more likely to behave in a malignant manner. However, the duration of the lesion does not always predict the subsequent biologic behavior.

Clinical signs of MCTs are due to the release of histamine, heparin and other vasoactive amines. Mechanical manipulation of the tumor during physical examination can induce degranulation leading to erythema and wheal formation and occasionally, an owner will report that the tumor appears to change in size over short periods of time. Gastrointestinal ulceration is also a potential complication of MCTs; between 35-83% of dogs with MCTs that underwent necropsy had evidence of gastric ulcers and plasma histamine concentrations were found to be elevated in dogs with MCT, primarily those with gross evidence of disease. Elevated histamine levels presumably lead to stimulation of H₂ receptors on parietal cells, excessive gastric acid production and the development of ulcers. Signs such as vomiting, anorexia, melena, and abdominal pain may be present.

Diagnosis

Cytologic evaluation of fine needle aspirates is probably the easiest method to diagnose the presence of a MCT. The mast cells appear as discrete round cells with a round to oval centrally placed nucleus that may be difficult to visualize due to the presence of granules. Mast cell granules may not stain with Diff-Quick, leading to difficulty in making a definitive diagnosis by cytology. Poorly differentiated malignant mast cells may contain few, if any, granules in which case special stains may be required. Other round cell tumors that should be included in the differential diagnosis include lymphoma, plasmacytoma, histiocytoma, and transmissible venereal tumor. While the diagnosis of a MCT can almost always be made by fine needle aspiration cytology, excisional biopsy is required for histologic grading of the tumor as grade is determined by multiple factors including cellular morphology and pleomorphism and degree of invasion into underlying tissues. It is important

to note that as wide surgical excision is the treatment most likely to cure the majority of MCTs, every effort should be made to obtain a definitive diagnosis via cytology prior to surgical intervention. As any cutaneous tumor may potentially be a MCT and dogs with this disease may have multiple tumors, fine needle aspiration should be performed on all masses prior to removal. If cytologic diagnosis proves difficult, a needle or punch biopsy of the tumor can be obtained prior to surgery. This may be preferable to a larger incisional biopsy, as local release of mast cell mediators will significantly inhibit healing, and may result in excessive bleeding.

Staging

Due to the fact that any MCT is capable of metastasis, all dogs with MCTs should be staged to determine the extent of their disease and overall health. This is particularly important for dogs in which radiation therapy may be utilized in the course of treatment.

Some or all of the following procedures may be indicated:

CBC, biochemistry profile, urinalysis

These tests are part of a minimum data base and should be included in the work-up of any animal suspected to have cancer. Dogs with MCTs (especially those with systemic disease) may have eosinophilia due to chemotactic factors and IL-5 produced by the mast cells. Anemia may be present secondary to hypersplenism or GI bleeding. Rarely, mast cells may be seen on a routine CBC.

Buffy coat smear

A buffy coat smear is made up spinning peripheral blood in a microhematocrit tube, breaking the tube at the buffy coat layer, and smearing the concentrated leukocytes on a slide. The buffy coat is then carefully examined for the presence of mast cells.

In summary, the buffy coat smear while easy to perform is probably not a very useful diagnostic test.

Bone marrow aspiration

In the normal bone marrow, mast cells are found infrequently. In one study, of 51 bone marrow samples examined, only 2 of these samples contained a single mast cell. It should be pointed out that these marrow samples were obtained from normal dogs, and it is possible that dogs with inflammatory disorders may exhibit higher numbers of mast cells in the bone marrow. In general, while bone marrow aspiration is a more likely to accurately detect systemic involvement than the buffy coat smear, it is usually easier to find evidence of such involvement in other organs (liver, spleen). Therefore, routine bone marrow aspiration is not recommended on most patients.

Lymph node aspiration

All regional lymph nodes should be carefully examined for signs of enlargement and any suspicious nodes should be aspirated for cytologic examination. Additionally, as metastatic nodes may palpate within normal size, it is recommended that all accessible regional lymph nodes be examined by aspiration cytology. Mast cells may be present in normal lymph nodes, and they are often found in reactive lymph nodes, so it may be difficult to determine if mast cells found on cytologic examination are neoplastic or part of the normal immunologic cellular repertoire. Indeed 24% of lymph node aspirates from normal beagle dogs contained mast cells. However, malignant mast cells in metastatic lymph nodes are often found in clusters/aggregates rather than singly, aiding in a diagnosis of metastasis. It is important to note that if possible, lymph node aspiration should be performed prior to surgical removal of a MCT, as post-operative inflammation can result in mast cell migration to local nodes and thus confuse the interpretation. If necessary, ultrasound can be used to identify the local lymph node of interest to facilitate needle aspiration.

Evaluation of the abdominal and thoracic cavities

Thoracic radiographs are always indicated as part of any staging procedure, although pulmonary involvement is uncommon in dogs with MCTs. Abnormalities reported include lymphadenopathy (sternal, hilar), pleural effusion, and anterior mediastinal masses, although these are rare. Evaluation of the abdominal cavity is important in dogs with MCTs, as spread to the liver and spleen, as well as other abdominal structures, may be noted. Ultrasound is a more sensitive diagnostic technique for evaluation abdominal organs. Any suspicious organ should be aspirated and examined by cytology. Some have recommended that splenic and hepatic aspiration be performed as part of the routine staging procedure, regardless of the presence of splenomegaly or hepatomegaly based on the fact that seemingly normal organs can have significant mast cell infiltration on cytology. However, as mast cells may be found normally in these organs, the utility of this procedure is not clear and sometimes results in confusion as to whether metastatic disease is present. Therefore, it is recommended that fine needle aspiration of the liver and spleen should be performed if abnormalities are detected in these organs during ultrasound examination, or if the dog possesses negative prognostic indicators.

Clinical staging system for canine MCTs

The following is the current clinical staging system for canine mast cell tumors:

0: single tumor, incompletely excised from dermis

I: single tumor, incompletely excised from dermis without regional lymph node involvement.

II: single tumor confined to the dermis with regional lymph node involvement.

III multiple dermal tumors or large infiltrating tumors, with or without regional lymph node involvement.

IV: any tumor with distant metastases or recurrence with metastases (including blood or bone marrow involvement).

Substage a: no signs of systemic disease

Substage b: signs of systemic disease.

Prognostic Factors

Canine MCTs possess a wide range of biologic behaviors, from benign to extremely aggressive leading to metastasis and eventual death from disease. Several prognostic factors have been identified that help to predict the biologic behavior of a MCT, as well as to direct the course of therapy.

Histologic Grade:

The histologic grade of a MCT is usually determined after excisional biopsy of the tumor, and cannot be assessed simply by cytologic evaluation of fine needle aspirates. The grade of a MCT is determined by the characteristics of the neoplastic cells (degree of granulation, cytologic and nuclear pleomorphism, etc). number of mitotic figures, and the extent of tumor invasion into the underlying tissues. Histologic grade is the most consistent prognostic factor and correlates significantly with survival, but it will not predict the behavior of every tumor. Furthermore, there is disagreement in tumor grading among pathologists; in one study there was significant variation among pathologist in grading the MCTs, although this was found to be less so if all pathologists strictly employed the system described by Patnaik.

Well differentiated tumors (Grade I): Are considered to behave in benign manner and complete surgical excision is usually curative. Historically, these represented between 30-55% of all mast cell tumors reported. Several retrospective studies have demonstrated that 75-90% of dogs are cured following definitive therapy. However, recently there is a trend toward fewer tumors being classified as Grade I, with most being placed in the Grade 2 category.

II Intermediately differentiated tumors (grade 2): these represent between 25-45% of all MCTs reported and their biologic behavior is more difficult to predict. On histopathology, they exhibit invasion into the underlying

subcutaneous tissue. As a result, they may be more challenging to remove by surgical excision. Historically, dogs with Grade 2 MCT have a reported mean survival time of 28 weeks after surgical removal, although the completeness of excision could not be assessed in this study. More recently, it has been shown that radiation therapy following incomplete excision of solitary Grade 2 MCTs can cure greater than 80% of affected patients, indicating that adjuvant radiation therapy clearly improves the survival times of dogs with those tumors. However, it is important to note that Grade 2

MCTs have the ability to spread to local lymph nodes, as well as distant sites, and a proportion of dogs that undergo definitive therapy (surgery and radiation) may go on to develop metastatic disease. Furthermore, some dogs that present with Grade 2 MCTs will already have evidence of metastatic disease making appropriate staging imperative for these dogs. Given the wide variation in biologic behavior among Grade 2 tumors there is now an effort to identify subcategories of Grade 2 tumors that may be more likely to behave in an aggressive manner using additional prognostic indicators described below.

III Poorly differentiated tumors (Grade 3): these tumors represent between 20-40% of all MCT reported. They often have in a biologically aggressive manner, exhibiting metastasis early on in the course of disease. The mean survival time of dogs with Grade 3 MCT has been reported as 18 weeks when treated with surgery alone. In one study, the percentage of dogs with Grade 3 MCTs surviving at 1500 days was reported as 6% and in another study, the percentage of dogs surviving at 24 months was 7%, indicating that these tumors are particularly malignant. With the recent addition of post-operative chemotherapy to the treatment regimen of Grade 3 MCT patients, evidence suggests that survival times may be improved.

Clinical stage:

Although the clinical staging scheme has been developed for prognostic purposes, each increase in stage (0-IV) has not necessarily been proven to worsen the prognosis. It has been demonstrated that when dogs are treated with radiation therapy, those with stage 0 MCTs survived significantly longer than did dogs with stages I-III MCTs. In that study, no dog had stage IV and therefore could not be compared for prognostic purposes. In two other studies, the presence of mast cells in the regional lymph node was a negative prognostic factor for survival and disease-free interval on univariate analysis suggesting that stage II has a worse prognosis than stage I. However, this may not be the case as an additional study revealed that dogs with Grade 2 lymph node metastasis treated with radiation post surgery achieved long-term survival. Lastly, while it would seem intuitive that dogs with multiple cutaneous mast cell tumors do not do well, two separate studies have demonstrated that this does not necessarily affect prognosis.

Anatomic location:

MCTs that develop in the oral cavity, nail bed, inguinal, preputial, and perineal regions were originally reported to behave in a more malignant fashion regardless of histologic grade. However, two reports now demonstrate that at least for definitive evidence for MCTs in the inguinal, preputial, and perineal regions this is likely to be untrue and dogs with tumors in these locations do not necessarily fare poorly. MCT that originate in the viscera (GI tract, liver, spleen), bone marrow or peripheral blood carry a grave prognosis.

Growth rate:

Tumors present for long periods of time (months to years) may be more likely to behave in a benign manner. In one study, 83% of dogs with tumors present for longer than 28 weeks prior to surgery survived for at least 30 weeks, compared to only 25% of dogs with tumors present for less than 28 weeks. The same study demonstrated that most dogs surviving for greater than 30 weeks postoperatively appeared to be cured.

Breed

Boxers have a high incidence of MCTs, but these tend to be more well differentiated and carry a better prognosis. However, every MCT should be treated as potentially malignant, regardless of breed.

Ki-67

Ki-67 is composed of 2 protein subunits that are present in cells during the active phases of the cell cycle, but absent during rest.

Mitotic Index

The mitotic index (number of mitoses per 10 high power fields) is often used as a prognostic indicator in other tumor types. A recent study suggests that mitotic index may be extremely useful for predicting the biologic behavior of canine MCT.

Treatment

The choice of treatment modalities utilized for a particular canine MCT depends heavily on prognostic indicators discussed above, especially the histologic grade and clinical stage.

Surgery

Wide surgical excision is indicated for all canine MCTs, as although they may feel like discrete masses, microscopically, most extend well beyond the palpable borders. Historically, it has been recommended that the margins need to be at least 3cm in each direction; deep margins are as important as the lateral margins. It is only recently that studies were conducted to try to quantify the amount of normal tissue required to achieve a complete excision. In two studies all of the Grade I MCT were completely excised with 1 cm of normal tissue around the MCT (lateral margins) and 1 fascial plane included in the excision (deep margin). In the same two studies, 75% and 68% of grade II MCT were completely excised with a 1 cm lateral margin and one fascial plane as the deep margin. Similarly, 100% and 89% of Grade 2 MCT were completely excised with a 2cm lateral margin and one fascial plane for the deep margin. Neither of the studies had Grade 3 MCT and therefore there are currently no data to make any kind of recommendations regarding margins for Grade 3 MCT. Clinically however, the diagnosis of MCT is often reached cytologically and a grade cannot be reliably assigned. Therefore the grade of the tumor is rarely known before the surgery. Because of this, it appears prudent to still recommend a 3cm lateral margin and one fascial plane for the deep margin when feasible. All of the excised tissue should be submitted; the lateral and deep margins should be accurately labeled so the pathologist is able to specifically identify any areas of incomplete excision. Careful examination of the histologic margins is imperative; however, even histologically clean margins do not guarantee that a tumor will not recur. This is particularly relevant for Grade 2 and 3 tumors, in which the underlying tissues may be involved. Part of the difficulty in evaluating tumor margins is that normal mast cells are present in all tissues, and it may be difficult for the pathologist to determine if a mast cell present at the tissue margin represents a malignant cell or a normal cell. In one study, 83% of dogs with Grade I MCT, 44% of dogs with Grade 2 MCT, and 6% of dogs with Grade 3 MCT were alive 1500 days after surgical excision. In another study, 100% of dogs with Grade I, 44% of dogs with grade 2 and 7% of dogs with Grade 3 were alive two years after surgical excision. Lastly, a proportion of Grade 2 tumors that are incompletely excised will NOT recur post surgery. In a recent study, the estimated proportions of Grade 2 tumors that recurred locally at 1, 2 and 5 years were 17.3%, 22.1% and 33.3% respectively. Eleven (39.3%) dogs developed MCT at other cutaneous locations. Median overall survival was 1426 days. The combination of Ki-67 and PCNA scores was prognostic for local recurrence and development of local recurrence was prognostic for decreased overall survival. Results suggest that a minority of incompletely excised MCT recur. Therefore, ancillary local therapies may not always be necessary.

Post surgical treatment recommendations are as follows:

Grade I-complete excision: no further therapy

Grade I incomplete excision: wider excision or radiation therapy if surgery not possible; may consider no further therapy

Grade II complete excision: Chemotherapy only if negative prognostic factors present

Grade II incomplete excision: wider excision or radiation therapy if surgery not possible; may consider no further therapy if there are no negative prognostic indicators; chemotherapy if negative prognostic factors present.

Grade III complete excision: chemotherapy

Grade III incomplete excision: chemotherapy +/- radiation therapy

It has been advocated that the injection of deionized water in the surgical site can decrease the likelihood of local recurrence after incomplete MCT removal. However, a more recent study found no benefit in the procedure and as such, the use of deionized water is currently not recommended.

Radiation Therapy

Substantial data suggest that radiation therapy is extremely effective at eliminating remaining microscopic disease following incomplete excision of Grade 1 and 2 MCT (greater than 90% three year control rate). Unfortunately, dogs with Grade 3 tumors do not fare as well; while the radiation may be effective at preventing local recurrence of tumor, many dogs eventually develop metastasis. Radiation therapy has also been used to treat solid MCTs (macroscopic disease) when surgery was not an option. Varying degrees of success have been found; in one study, a fifty one year control rate was obtained using total doses of 45 to 57 Gray. However, radiation therapy should not be utilized as the primary therapeutic modality if surgical intervention is an option. Palliative radiation has also been utilized to treat dogs with non-resectable high grade MCT. This may result in an improvement in quality of life, but is unlikely to significantly increase survival time. Moreover, systemic effects of mast cell degranulation following radiation may lead to vomiting, hypotension and GI ulceration.

Chemotherapy:

The use of adjuvant chemotherapy is indicated following excision of Grade 3 MCTs, metastatic MCTs, non-resectable high grade tumors, or for any other MCT with negative prognostic indices. While radiation therapy, is considered the treatment of choice for incompletely excised Grade I and 2 MCTs, evidence now suggests that post operative chemotherapy may prevent local recurrence and therefore should be considered for patients who are not candidates for radiation therapy or if such therapy is not available or if the owners simply cannot afford the cost. In general chemotherapy for bulky MCT has for the most part been unrewarding and long term responses have not been demonstrated in well controlled clinical trials.

Corticosteroids: The exact mechanism of how corticosteroids kill malignant mast cells is not known. The reported response rate of canine MCT to prednisone is 20% with remission times of 10 to 20 weeks. Partial remissions are more common than complete remissions, and at least some of the observed response may be due to a decrease in tumor associated edema.

CCNU (lomustine):

An alkylating agent that has been used to treat lymphoma and brain tumors in dogs, CCNU was recently found to have activity against canine MCT. A response rate of approximately 42% was noted when dogs with Grade 2 and 3 MCTs that had failed all other therapies were treated with CCNU. As with prednisone, most of these were partial responses, and the duration of response was only 79 days. However, it does appear that this drug has some efficacy in treating MCT, and clinical trials are currently underway to further evaluate its efficacy. Preliminary data suggests that CCNU given in the adjuvant setting post surgery (either alone or with prednisone and vinblastine) can significantly prolong survival times of dogs with high grade tumors or tumors with negative prognostic indicators. It should be noted that CCNU can produce both hematopoietic and hepatic toxicity including severe neutropenia, thrombocytopenia and liver failure.

Vinblastine: Vinblastine has been reported to have efficacy against canine MCT in two separate studies. In the first study, dogs with Grade 2 or 3 MCT with metastasis to the regional lymph node underwent surgical removal of the primary tumor and involved lymph node. They were then treated with combination of vinblastine, prednisone, and cyclophosphamide, resulting in a median survival time of 18 months.

Miscellaneous drugs: In limited clinical reports, both L-asparaginase and chlorambucil have been found to have activity against MCT. Inhibitors of Kit have recently been demonstrated to have clinical activity against canine MCT in two separate studies and clinical trials with such inhibitors are ongoing. Evidence suggests that they may be particularly useful for dogs with tumors exhibiting Kit mutations, especially in the adjuvant setting.

Supportive Care

Animals with large primary MCT, evidence of metastatic disease or systemic signs should be treated with medications to block some or all of the effects of histamine release.

H2 antagonists: As histamine stimulates gastric acid production by parietal cells, MCT may cause GI ulceration. To prevent this, any of the standard H2 antagonists may be utilized including cimetidine, ranitidine, or famotidine.

H1 antagonists: Massive mast cell degranulation can lead to hypotensive shock and death. Therefore all patients with gross mast cell disease should be placed on the H1 antagonist diphenhydramine.

Miscellaneous: Treatment with sucralfate is indicated for dogs with evidence of GI ulceration. Cyproheptadine stabilizes mast cells and may be useful in the treatment of dogs with bulky mast cell disease.

GENERAL NOTES:

Canine Cancer mimics Childrens Cancer

1. Identify the type Cancer (needle Biopsy/aspirate)
2. Stage the Cancer--determine if the cancer has spread
3. Make a treatment plan....surgery/chemo/radiation/clinical trial--new therapy.

Diagnosis of Cancer: Needle aspirate

Carcinoma

Lymphoma Sarcoma

Punch Biopsy

Needle biopsy

Determine

How extensive is the tumor--physical exam, imaging--CT/MRI

Has the tumor spread...Exam lymph nodes

Chest X-ray--tumor has to be 9mm to be seen on XRAY

1mm size for Cat scan

Ultra sound--easier to locate masses

Treatment depends: type stage health of the patient, financial considerations

Primary Treatment

1. Surgery--curative if not spread. Easiest when small..plan surgery in advance to insure the best chance of getting the entire tumor.
2. radical surgeries are easier as pets don't have the same cosmetic concern as humans...advanced pain control
3. Many tumors need at least 1 to 2 inches of normal tissue as a margin to ensure all of the tumor cells have been removed.

Chemo--works best in setting of minimal disease--post surgery--to treat potential spread of tumor.
Exact type and duration of chemo is dependent on the type of cancer.

Chemo:

1-3 weeks given--some can be given orally but most are given by injection

Administration in 1-2 min. into a vein with minimal discomfort.

Side effects: low white blood cell count

Nausea/vomiting. Diarrhea, hair loss--not common (except in Old English)

Only 5-10 % of patients have significant side effects.

Radiation--Given following surgery to kill off any remaining cells. In most cases small dose one time a day
3-4 weeks.

Provide pain relief if bone tumor

Used to eliminate residual disease.

Side effects: slight skin burn--will heal 2-3 weeks.

Advances in therapy:

Cancer develops spontaneously

Heterogeneity of cancer cells and blood supply

Genetic instability--chromosome abnormality and mutations of genes

The tumor spread (metastasis) is common

Dogs have a higher incidence of some types of cancers: Osteo, soft tissue and Sarcomas.

Approx. 8,000 dogs per year get osteo.

Genetic factors contribute to cancer. Several breeds of dogs are at risk for developing cancer: Greyhounds, Rottweilers (osteosarcoma) Scottish Terrier--bladder cancer.

Efforts are underway to identify genetic factors: The comparative Oncology Program.

Immune Stimulation:

Goal is to stimulate the immune system to recognize and destroy cancer cells

Approaches: Tumor vaccines--gene therapy.

Humans: Herceptin-antibody therapy for breast Cancer

Rituxan antibody therapy for lymphoma

Cytokines IL-2 + IL-12 for kidney tumors

Dogs: Vaccines--melanoma--1st vaccine DNA based vaccine for canine melanoma--In 2007--use dogs post surgery by Board Certified Oncologists--Should be out Jan/Feb.

Immune --melanoma , hemangio, osteo

Angiogenesis--growth of new blood vessels..normal process that takes place during wound healing

Anti Angiogenesis--goal inhibit the growth of blood vessels into tumors

Cancer can make own blood vessel cells.

Development of Sutent

2001-2003--Clinical trial

3 cures, 28% response

Used in humans with similar response.

Novel Therapy

Sutent ---\$3,000 per month

Signs

Be aware of any changes: loss appetite, decreased energy, weight loss

Check animal regularly--make sure to look into the dogs mouth

Yearly health exams are important

Give your vet a detailed history...always get a diagnosis (fine needle biopsy)

Consider ALL options

Early intervention is important!

Larger Breeds: place increase weight on bones...cause more remodeling and chronic remodeling of cells -- grow and mutations occur.

50-20% of all osteo sarcoma is in Rottweilers--

Immune Response

Mast Cell Biology--mast cell has normal biological function--detect virus..response to bacteria

Derived from bone marrow . precursors Leave marrow and immature state and migrate to many tissues.

Most common skin tumor of dogs--mean age 8-9 years

Etiopathogenesis is unknown

Mutations found in 30% malignant canine MCTs

MCTs occur after birth--not inherited

Occurs subcutaneous --rarely systemic

MCTs can look like anything...

To diagnose:

1. Fine needle aspirate
2. biopsy--try to avoid--only if cytology is non diagnostic--promotes bleeding and swelling

Staging

1. CBC, bio chem. Profile, UA
2. Buffy coat smear
3. Bone marrow aspirate--usually found other places first
4. lymph node aspirate
5. evaluation of thorax and abdomen

Histologic grade--most consistent prognostic factor--Incisional or excisional biopsy--not by cytology

Grade 1 Well granulated..do not invade into underlying tissue

Grade 2 most of what you see 75% ..many are benign, but will invade into muscle and subcutaneous

More difficult to remove

May be metastatic and may lead to systemic disease