

Lymphoma (Lymphosarcoma)

by Pamela A. Davol

Cells derived from the bone marrow that mature and take part in cellular immune reactions are called lymphocytes. When lymphocytes undergo transformation and become cancerous cells, they may invade the bone marrow and cause lymphocytic leukemia, or they may invade the organs of the lymphatic system (lymph nodes, thymus, spleen) and form solid tumors within these organs called lymphomas (also called lymphosarcomas). Lymphomas may originate from T-lymphocytes (lymphocytes processed by the thymus gland which take part in hypersensitivity and immune-rejection) or from B-lymphocytes (lymphocytes independent of the thymus which play a role in circulating antibody production). Lymphocytic cancers are the third most common tumor-type occurring in the dog. Of the different forms of this kind of cancer, lymphoma is the most common, accounting for 5-7% of all tumors seen in the dog and affecting as many as 24 out of every 100,000 dogs. Lymphoma occurs in all breeds but may have a higher incidence in Boxers, Dobermans, Golden Retrievers and Scottish terriers. There is no evidence that either sex has a higher risk for development of lymphoma, although some evidence suggests females that develop lymphoma may have a longer survival duration than males similarly diagnosed.

Average Age of Onset

Lymphoma may occur in dogs of any age but is seen more frequently in dogs over 5 years of age.

Cause

Malignancies originating from lymphatic cells have been shown to be of viral origin in a number of animals, however, no virus has yet been identified in association with this disease in the dog. However, recent findings have identified the presence of a virus, which reportedly has similarities to the feline leukemia virus, in the lymph nodes of a dog with an immunodeficiency disorder. In a separate report, researchers identified germ-line (hereditary) abnormalities of a gene encoding a specific tumor suppressor protein as being present in the cells of dogs with lymphoma. In light of these findings, it is suspected that transformation of lymphatic cells is dependent upon the initial presence of compromised lymphoid tissue due to genetic defects, radiation exposure, immunosuppressive agents, or immune system abnormalities that predisposes the dog to environmental carcinogens.

Symptoms

There are four forms of lymphoma that may develop in the dog. General symptoms of all forms of lymphoma include fever, weight loss and anorexia (loss of appetite). Specific symptoms are dependent upon which form the dog develops. 1)

Multicentric lymphoma is a diffuse form with wide-spread

involvement of lymph nodes and lymphatic organs. Dogs will present with enlarged, painless lymph nodes in the neck (cervical nodes), under the front legs (axillary nodes) and in the groin (inguinal nodes). It is not unusual for these nodes to enlarge to the size of golf balls or even baseballs virtually overnight in the case of this disease. Enlargement of the tonsils may obstruct swallowing and obstruction of lymphatic drainage by the tumor may cause fluid build-up and swelling of the face and legs. The spleen is often enlarged. 2) Alimentary lymphoma occurs in the digestive tract. Growing tumors may cause obstruction of the processing and passage and present symptoms of vomiting and diarrhea. These symptoms may be intermittent in the early course of the disease and progress in severity with the disease. Often, these dogs also become emaciated (abnormally thin) because the diseased gastrointestinal tract is unable to absorb protein and nutrients during digestion. 3) Mediastinal lymphoma (developing in the center of the chest usually associated with the thymus gland) is a rare form of lymphoma in the dog. Dogs with this form of lymphoma show signs of easily being fatigued and have respiratory symptoms such as difficulty breathing. 4) Cutaneous lymphoma affects the skin but may also involve superficial lymph nodes. This form of the disease appears as a number of raised lesions or pale plaques that invade the skin.

Diagnosis

Biopsy and microscopic examination of the lymphoid tissue are

required for accurate diagnosis of lymphoma in early stages. Fine-needle aspiration for the purpose of biopsy is often not sufficient for diagnosing this form of cancer. Additionally, during the early stage, laboratory blood work may be within normal values and provide little help in patient evaluation. In more advanced stages of the disease, white blood cell count may be elevated and cancerous lymphocytes may be detected in the blood. In many advanced cases, radiographic evidence of chest and/or abdominal masses in the presence of widespread lymph node enlargement may preclude the necessity of biopsy.

Treatment

Combination chemotherapy, which is a treatment regimen where the dog is administered two or more drugs on a particular schedule, is the standard therapy for lymphoma. Clinically, the most effective treatment regimen, called UW-M, has resulted in response rates (tumor regression) as high as 91% for periods of 6 months or more. This regimen uses a combination of 5 drugs (Vincristine, L-Asparaginase, Prednisone, Cyclophosphamide and Doxorubicin), administered over a nine week period. If this initial treatment schedule is successful in producing remission of the disease, then this treatment is followed by a maintenance drug schedule, which ideally continues for up to 2 years.

Single-agent therapy with Doxorubicin alone or Prednisone alone also produces remissions, albeit with shorter durations,

in some dogs and provides a more convenient treatment schedule for pet owners.

Immunotherapy with a monoclonal antibody (Mab 231) that specifically recognizes some canine lymphomas has been used successfully following chemotherapy for the purpose of prolonging disease remission.

Conventional radiation therapy has been found to be ineffective against lymphoma. However, clinical studies exploring radiation therapy with bone-marrow transplant in dogs indicates a possible therapeutic gain may be achieved by combining these two methods.

Prognosis

Without therapy, dogs diagnosed with lymphoma succumb to the disease within 4-6 weeks following diagnosis. There is strong evidence to suggest that lymphomas developed from T-lymphocytes are more aggressive and bear a poorer prognosis than those developed from B-lymphocytes. Treatment produces tumor remission in approximately 90% of cases, with duration of remission and survival dependent upon the treatment regimen used. Use of Prednisone alone helps to improve quality of life, however, remissions are brief, lasting only about 30 days. Combining Cyclophosphamide with Prednisone may provide a slightly longer duration of remission (30-60 days). Treatment with Doxorubicin alone has produced remissions for up to 18-29 weeks. A recent study indicates that monitoring plasma glutathione-S-transferase may be helpful in evaluating therapeutic response to doxorubicin

treatment. The UW-M protocol (described above) has demonstrated the longest durations of remissions lasting 44-69 weeks for early stage lymphomas and 36-51 weeks for more advanced lymphomas.

Prevention

Considerable evidence links development of lymphoma with defects in or suppression of the immune system. Therefore, prevention of lymphoma may lie in efforts to protect predisposed dogs with immunodeficiency or auto-immune diseases from exposure to environmental carcinogens that increase likelihood of cancer development. Additionally, frequent use of immunosuppressive drugs may also increase risk of lymphoma reprinted with permission. Pamela A. Davol, 76 Mildred Avenue, Swansea, MA 02777-1620. (508) 673-0631 [Pamela Davol](#)