

Canine Lymphoma

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Lymphoma is one of the most common neoplasms in middle aged dogs. The annual incidence is 24 cases/100,000 dogs at risk. Lymphoma in dogs is more common than in people but less common than in cats. The etiology of lymphoma is unknown but there are a multitude of hypotheses suggesting that viruses, genetics, herbicides, and/or magnetic field exposure may be involved. Breeds at high risk include Boxers, Bassett Hounds, St. Bernards, Scottish Terriers, Airedale Terriers, and Bulldogs. Also, certain breeds tend to develop B-cell lymphoma (Bassett Hounds, Cocker Spaniels, Dobermans, Scottish Terriers, Rottweilers) whereas others develop T-cell lymphoma (Airedale Terriers, Cavalier King Charles Spaniels, Shih Tzus, Huskies).

Classification of malignant LSA in dogs can be distinguished on the basis of anatomic location, histologic criteria, and immunophenotypic characteristics. The anatomic forms of lymphoma include multicentric (80-85%), gastrointestinal (5-7%), cutaneous or mycosis fungoides (5%), mediastinal (2-5%), and extranodal (7%). Clinical signs include weight loss, anorexia, lethargy, vomiting, diarrhea, and PU/PD. Other clinical signs may be specifically related to the site of involvement. Physical examination findings may include lymphadenomegaly, hepatosplenomegaly, cachexia, and/or fever.

Diagnosis of lymphoma can be attained with a lymph node aspirate +/- a lymph node biopsy. A CBC, chemistry profile, and urinalysis should also be performed before treatment is started. Hematologic abnormalities with lymphoma may include anemia, thrombocytopenia, neutrophilia, lymphocytosis, hyperglobulinemia, hypoproteinemia, increased transaminases, azotemia, hyperbilirubinemia, and hypercalcemia. Proteinuria may be identified on urinalysis. Staging tests include thoracic and abdominal radiographs, abdominal ultrasound, +/- bone marrow aspirate and immunophenotyping (on lymph node tissue or aspirate).

The World Health Organization (WHO) classifies lymphoma using the following schematic:

- **Stage I: Single node**
- **Stage II: Regional nodes**
- **Stage III: Generalized nodes (cross diaphragm)**
- **Stage IV: Liver/Spleen involvement (+/- I-III)**
- **Stage V: Bone Marrow involvement (+/- I-IV)**
substage a= no clinical signs, b=ill, high Ca⁺⁺

Some recently developed tests that can be utilized to differentiate between a neoplastic proliferation of lymphocytes and a reactive proliferation of lymphocytes include flow cytometry and PCR for antigen receptor rearrangement (PARR). Flow cytometry detects antigens on cell surfaces (CD3, CD5, CD4, CD8= T cell; CD 21= B cell) and can be performed on peripheral blood, lymph node aspirates, cellular masses, and effusion. This test has limited use in felines.

The PARR test is used to detect clonality of cells. In a T-cell neoplasm, all cells should have the DNA sequence of a T-cell receptor gene. Likewise, cells within B-cell lymphomas should have identical DNA sequences for a B-cell receptor gene. A reactive population of cells will contain polyclonal antigen receptors. The PARR test is 80% sensitive in dogs and 94% specific. In cats the test is 65% sensitive. This test may be performed on lymph node aspirates, peripheral blood, spleen aspirates, bone marrow aspirates, CSF fluid, and non-cellular masses. Both flow cytometry and the PARR test are currently performed at Colorado State University and the University of California.

The mainstay of therapy for lymphoma is chemotherapy. Drugs commonly used include prednisone, vincristine (Oncovin), cyclophosphamide, doxorubicin (Adriamycin), L-asparaginase, methotrexate, mitoxantrone, and lomustine (CCNU). A cure for lymphoma is rare but the remission rate is generally high (70-90%). With no treatment the average survival time is 4-6 weeks. With prednisone therapy alone, side effects are more common, but a 2-3 month remission time may be attained. Treatment with the COP protocol (cyclophosphamide, vincristine, and prednisone) yields an average remission time of 6-7 months. Although multi-drug protocols require greater cost, increased risk of toxicity, and increased number of visits, they are more effective in producing a longer average remission time (~9 months) and overall survival time (12-17 months). Strong prognostic factors associated with remission and survival time include immunophenotype (T-cell lymphomas are worse than B), substage (b worse than a), histological grade, location (CNS, mediastinal, GI, CNS, leukemic worse), and prior treatment with prednisone.

Radiation therapy is considered for local Stage 1 or 2 disease (nasal lymphoma or CNS lymphoma). Radiation may also be considered for palliation of local disease such as rectal lymphoma or mediastinal lymphoma. Staged half body radiation with chemotherapy has also shown promising results for treatment of lymphoma. The use of whole body radiation therapy with bone marrow transplant has yielded poor results.

Feline Lymphoma

The incidence of feline lymphoma is very common with 200/100,000 cats at risk affected. Classification is determined by anatomic location, histologic type, cytologic type, and immunologic type. The different forms of lymphoma in cats include alimentary (50-70%), multicentric (10-25%), mediastinal (10-20%), nasal (10%), and renal (5-10%). Feline leukemia

virus (FeLV) positive cats with lymphoma are more likely to be young cats with mediastinal or spinal lymphoma. Most cats with alimentary lymphoma do not have the virus.

Clinical signs in cats are dependent on the site of involvement. Cats with gastrointestinal lymphoma may present with a history of weight loss, anorexia, diarrhea and/or vomiting. Mediastinal lymphoma may cause dyspnea, tachypnea, and Horner's syndrome. Nasal lymphoma may cause respiratory stertor and nasal discharge.

As with dogs, chemotherapy is the mainstay of treatment for feline lymphoma. However radiation therapy may also be utilized for mediastinal or nasal lymphoma. In general cats have a 50-60% remission rate with multidrug chemotherapy. Average survival time is typically about 6-10 months. In one study, cats with low grade small cell intestinal lymphoma had an average survival time of 17 months when treated with a combination of prednisone and chlorambucil. In general, prognostic factors for survival time include response to therapy, histologic grade, FeLV status, and location of the disease.

References Available Upon Request