What a veterinarian in practice needs to know about lymphoma in dogs

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I was told that in New York City with its large number of veterinary specialists that most dogs with lymphoma were referred to oncologists for treatment. This presentation will focus on the initial diagnostics and prognostic information that the owner may need before deciding to be referred to an oncologist.

Diagnostics

Many dogs with **B-cell lymphoma** have generalized lymphadenopathy as the presenting sign noted by the owners. General well-being is good in most dogs. Aspiration cytology of an enlarged lymph node is the easiest route to diagnosis but there are things that need to be considered:

Avoid aspirating a lymph node in the area of inflammatory disease such as a mandibular lymph node in a dog with advanced dental disease.

Malignant lymphocytes are especially fragile and squash preps of aspirates will often break down the malignant cells making diagnosis difficult to impossible.

Making cytology slides using the same technique as blood smears is a gentle approach.

Make thin preparations that are easier for the pathologist to interpret.

Other causes of lymphadenopathy are: fungal infections, toxoplasmosis, auto-immune diseases, inflammatory reactions, mast cell tumors and metastatic tumors. Aspiration cytology is helpful in differentiating these possibilities.

Dogs with **T-cell lymphomas** usually have less prominent external lymph nodes or don't have involvement of external lymph nodes. Thoracic and abdominal involvement of the lymphoma requires radiographs and ultrasound guided aspirates for diagnosis. Sixty to seventy percent of dogs with lymphoma have thoracic lesions but rarely have lung nodules. Tracheobronchial and sternal lymph nodes may be enlarged and diffuse interstitial lesions in the lungs may be seen as well as anterior mediastinal mass(es).

Dogs with T-cell lymphoma are often sick with anorexia, polyuria and polydipsia, vomiting and diarrhea. Hypercalcemia or infiltration of liver and kidneys may produce these signs. Hypercalcemia may produce profound anorexia before other signs develop. Muscle weakness is often seen with high serum calcium levels. Hypercalcemia is commonly seen in dogs with T-cell lymphoma. Identification of hypercalcemia provides a focus to the work-up of the case. Hypercalcemia of malignancy is the most common cause of hypercalcemia of the middle age or older dog. T-cell lymphoma and anal sac carcinoma are the most common causes of hypercalcemia of malignancy but a variety of other tumors can cause hypercalcemia. A rectal examination will usually identify an anal sac carcinoma. Rodenticides and parathyroid tumors can cause hypercalcemia. Dogs with parathyroid tumors can be hypercalcemic for a long time without showing clinical signs but hypercalcemia of malignant rapidly causes renal failure.

Immunophenotyping

The characterization of the lymphoma as a B-cell or T-cell lymphoma can be made by immunophenotyping with specific antibodies using flow cytometry. This will give the percent of B and T cells in the lymphoma. Subtypes of T-lymphocytes can be determined using antibodies to CD4 and CD8 markers. This can also be done by immunohistochemistry of a lymph node biopsy. To do flow cytometry, the laboratory requires 3 or 4 needles filled with cells taken from the abnormal lymph nodes.

Lymph node enlargement without a definitive diagnosis on cytology.

Some low grade lymphomas or indolent lymphomas cannot be consistently diagnosed from cytology and require a biopsy and immunophenotyping for diagnosis. Marginal zone lymphomas, follicular lymphomas and B and T small cell lymphoma fall in this category. If the lymph node contains a homogenous population of lymphocytes, the diagnosis of lymphoma is likely. Clonal assays can be helpful in differentiating benign lymphoid hyperplasia from lymphoma. Clonal expansion from one cell is a characteristic of malignancy. Using PCR techniques to amplify DNA of the B-cells immunoglobulin gene or in T-cell lymphomas the genes for the variable region of the T-cell receptor gene will identify clonality. A false positive reaction can occur in dogs with Ehrlichiosis that can have a monoclonal gammopathy.

Thymidine Kinase test correlates with cell turnover and has been suggested as a diagnostic test for lymphoma and hemangiosarcoma. I have concerns about this test because I would not start chemotherapy on the findings and would be concerned about doing a lot of advanced diagnostic for a positive test.

Leukemias

Chronic lymphocytic leukemia (CLL) is a type of lymphoma with large numbers of small normal looking lymphocytes. It is usually identified as an incidental finding in dogs being worked up for routine procedures such as dentistry. The clinical pathologist will have a strong suspicion of CLL from the blood smear. Lymphocyte counts of > 30,000 cells/ul are commonly seen. CLL can be associated with auto-immune anemia, pure red cell aplasia and monoclonal gammopathy. This has a good prognosis with many dogs living over 2 years.

Acute lymphoblastic leukemia (ALL) has lymphoblast in the circulation usually accompanied by neutropenia and thrombocytopenia. The severe neutropenia may preclude treatment with many of the chemotherapy agents. This has a terrible prognosis.

Stage V lymphoma occurs in dogs with extensive multicentric lymphoma that involves the bone marrow resulting in circulating lymphoid cells. This has a guarded prognosis but may respond for a while to chemotherapy.

Prognostic factors

B cell lymphomas do better (median survival times of 389 day with 50% alive at a year and 20-25% alive at 2 years) compared to T cell lymphomas with a median survival time of about 160 days.
Sub-stage b lymphomas (sick dogs) do worse than dogs that are not sick.
Stage III, IV and V lymphomas do worse than Stage I and II lymphomas.
GI lymphomas do worse than multicentric lymphomas.
Indolent or low grade lymphomas don't respond well to chemotherapy but can live a long time.
Previous treatment with steroids significantly reduces survival times with subsequent chemotherapy.
Steroids promote the development of multiple drug resistance in the lymphoma.
Breeds like Collies and Shelties may have mutations (ABCB1 mut/mut) in the MDR (multiple drug resistance gene) that increases toxicity not only to ivermectin but also to some chemotherapy agents.