Lymphocytic Leukemia in the Canine Patient

Lymphocytic leukemia is the most common of all the leukemias to affect canine patients. It is a nebulous disorder that can cause confusion for general practitioners and specialists alike. The disease can present in two general forms: acute lymphoblastic leukemia and chronic lymphocytic leukemia. Recognizing this disease, diagnosing it, and differentiating between the two forms is important for the treatment, prognostication, and management of the disease.

While no true incidence has been reported, we believe that German Shepherd Dogs and Golden Retrievers may be overrepresented. Lymphocytic leukemia typically occurs in older dogs. Causes are largely unknown, but retroviruses, like the Feline Leukemia virus, have been implicated in other species like cats and people.

Chronic lymphocytic leukemia (CLL) tends to occur in larger dogs. The typical presentation includes a healthy geriatric animal that presents for pre-anesthetic bloodwork or routine annual examination. The disease course is insidious and typically indolent. Often the only finding is an elevated lymphocyte count on a routine CBC. However, some owners will report lethargy and a decrease in appetite. Patients with counts over 30,000/μL will often have other abnormalities in their bloodwork such as thrombocytopenia, anemia, or neutropenia. CLL is a monoclonal expansion of one cell population. This single T cell, B cell, or atypical lymphocyte will clonally expand and produce the lymphocytosis. While this fact may seem purely academic, it becomes a relevant fact that is exploited for diagnostic purposes and will be discussed later. The majority of canine CLL is of T cell (granular lymphocyte) phenotype. This means that the cell membrane will carry a CD8+ marker. The second most common phenotype is B cell, followed by an atypical phenotype.

Diagnostics that can confer that your patient has CLL include bone marrow aspirate, flow cytometry, cytopathology, and PARR (PCR for Antigen Receptor Rearrangement). A blood smear of a patient with CLL will contain a plethora of abnormal circulating lymphocytes. The lymphocytes often include small pink granules. This would be an excellent indication to have a boarded pathologist examine your slides. Morphology can help determine the type of leukemia your patient has, and this will strongly influence prognosis and treatment. Bone marrow aspirate is particularly relevant if you note “penias” in your CBC. As the disease progresses, myelophthisis occurs and neoplastic cells will crowd out the normal bone marrow constituents. Bone marrow aspiration is not always positive for cancer in patients with CLL. Often this disease will originate in other lymphoid organs, like the spleen, and only later will it travel to the bone marrow.

Other diseases such as hypoadrenocorticism, chronic antigenic stimulation from a bacterial infection, fungal diseases, and Rickettsial diseases such as ehrlichia, or Rocky Mountain Spotted Fever can cause a lymphocytic proliferation in the peripheral blood. Being able to determine the source of this increase can be challenging. Flow cytometry or PARR can aid in determining whether these populations are a monoclonal expansion and what type of cell is the culprit (B vs. T cell). Typically, other etiologies of lymphocytosis will cause a polyclonal expansion of cells. Exceptions, of course, always exist. Flow cytometry works by sorting cells through a laser, similar to how your CBC machine works. It determines the size and complexity of each cell. Cells that are monoclonal will all look exactly the same. Fluorochromes, or fluorescent markers, can then be added to determine cell membrane
markers. Again, if they are all the same it is likely a monoclonal expansion of cells. Samples of peripheral blood can be sent off to determine clonality and phenotype.

PARR is a test that will also determine clonality. A clonality assay is a test that will determine if all cells are derived from a single clone, as is the case in leukemia. PARR uses the variable epitope on the heavy chains of antibodies to determine clonality. Remember that the shape of the antibody is such that each end of the antibody has a “variable region”. This region is responsible for recognizing different antigen in the body. An expansion of lymphocytes that results from infection should cause different variable regions to recognize different components on the antigen. You will get lots of cells but they will all be different. PARR chops up the antibody on these cells and determines if the variable region is all the same or if they are different. PARR will give you an evaluation of the clonality of your cells, but it is less good at figuring out phenotype (who the cells are). PARR can be run on blood smears that are already stained. This test is not 100% specific or sensitive and cases can be misdiagnosed or missed.

Prognosis for CLL is typically excellent. Often animals do not require therapy after the initial diagnosis until lymphocyte counts start to markedly increase. In the literature, dogs with a T cell-CLL had a prognostic indicator at 30,000 cells/uL. Dogs with lymphocyte counts greater than 30,000 lived an average of 131d. Dogs who presented with a lymphocyte count of less than 30,000 lived an average of 1098 d. Treatment typically consists of an oral chemotherapy protocol. Prognostic indicators for dogs with B cell-CLL, are cell size. Dogs with large cell B cell-CLL have a median survival time of 129 d where as dogs with medium or small sized B cells did much better.

Acute lymphocytic leukemia (ALL) typically has a different presentation. These dogs often present with clinical signs of weight loss, anorexia, and lethargy. Often these patients have organomegaly and lymphadenomegaly on physical examination. CBC results often show signs of severe myelophthisis of the bone marrow. Secondary bleeding tendencies are not uncommon. The diagnostic tests are similar to that of the CLL patient, however bone marrow infiltration is often severe. Diagnostics such as PARR and Flow cytometry are also useful in determining the diagnosis as well as the treatment regimen.

The majority of ALLs will be of B cell origin. ALL is determined if >30% of the cells in circulation are lymphoblasts. The more immature the cell that underwent clonal expansion, the worse the prognosis is for the dog. Flow cytometry can aid in helping owners make decisions. CD34 is a marker on the cell membrane of very immature bone marrow progenitor cells. Flow cytometry can determine if this marker is present on the lymphoblasts. CLL will not have this marker present. If a patient has CD34+ ALL the median survival time is 16 days. Treatment of ALL requires aggressive injectable chemotherapy protocols.