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FELINE LYMPHOMA

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Lymphoma (LSA) is one of the most common feline malignancies, comprising approximately 30% of all reported tumors. While not curable, LSA may respond quite well to therapy and can be a very satisfying neoplasm to treat. Importantly, the treatment for lymphoma varies depending on whether the disease is characterized as lymphoblastic or lymphocytic.

**Lymphoblastic lymphoma**

The age of cats affected has increased over the past 10 years, due to the decline in FeLV+ cases. Middle-aged to older cats are mainly affected. Young cats with LSA are often FeLV+.

FeLV is linked with most forms of LSA except the GI form. FeLV+ LSA is a T cell variant and occurs in younger cats (2 to 4 years). The risk of developing LSA is increased by 5x with FIV infection and by 77x with FeLV and FIV co-infection. FeLV can directly cause malignant transformation, while FIV is thought to predispose to lymphoma via immune dysfunction. Inflammatory bowel disease may ultimately progress to lymphoma, but this theory is not proven.

Presenting complaints in cats depends on the form of LSA affecting the patient. As the GI form is the most common, signs include any or all of the following: weight loss, inappetance, lethargy, vomiting, and/or diarrhea. Multicentric cases will usually be ill and have enlarged lymph nodes (“lumps” noted by owner). Mediastinal LSA causes dyspnea (from the mass or secondary pleural effusion) and/or regurgitation (also a mass effect). Extranodal LSA also will present with concerns based on location: sneezing/epistaxis for nasal, paresis/paralysis for CNS, systemic illness with the renal form, and blindness or discomfort in ocular cases.

Depending on the form of the cancer, the diagnosis of LSA may be achieved with fine needle aspirate (FNA) or it may require histopathology. Situations where biopsies are indicated include the GI form that is typically microscopic and diffuse, multicentric lymphoma (peripheral lymph nodes can be enlarged for a
number of non-neoplastic causes which may not be cytologically distinguishable), nasal and cutaneous LSA.

As LSA is almost always a systemic disease, staging to determine extent of disease is important for prognosis and monitoring response to therapy. Most of the specific forms of LSA do not stay isolated to the primary location. For example: GI lymphoma typically involves multiple sites along the intestine, renal LSA may progress to involve the CNS, and spinal LSA frequently involves the bone marrow. Conversely, nasal and/or nasopharyngeal lymphoma in cats is reportedly often isolated to just the one site, and thus these sites may be effectively treated with radiation therapy.

Diagnostic evaluation should include a complete blood count, serum chemistry profile, urinalysis, FeLV/FIV testing, bone marrow aspirate, thoracic and abdominal radiographs and abdominal ultrasound. Clinical substage is based on presence of symptoms: substage ‘a’ is asymptomatic, substage ‘b’ correlates with an ill patient.

Unlike dogs, there are not many prognostic factors in cats that help to predict which cats will respond to therapy. The anatomic location of the lymphoma may be prognostic; some forms may respond better than others. In this authors experience, patients with stage I lymphoma tend to live longer than patients with diffuse disease. Further, cats with renal or CNS involvement tend to do more poorly overall. Prognostic information is somewhat unclear due to most studies grouping together cats with various forms in the remission/survival analysis, and due to small numbers of cats in the studies. Other prognostic factors include clinical substage (b does worse) and FeLV status (+ have decreased remission times). One of the most prognostic findings, which unfortunately cannot be assessed prior to treatment, is response to therapy (cats that go into remission have greatly prolonged survivals).

Overall, cats tolerate chemotherapy well. The most common side effect is anorexia (~20%), but even that is usually not severe and is usually short lived. Neutropenia may occur, but is fairly rare with the chemotherapy used for lymphoma. Cats will lose their whiskers and their guard hairs – leading to a soft, fluffy coat. Constipation may be seen, particularly with vincristine. Renal function needs to be monitored with doxorubicin administration; cumulative doses up to 150 mg/m2 are generally well-tolerated but the BUN, creatinine and urine specific gravity should be monitored monthly to every other month in these patients following completion of therapy as cats may experience renal failure as a late side effect of doxorubicin.

In spite of the risk of renal failure, protocols containing doxorubicin are recommended as they lead to increased remission rates and survival times in cats with LSA as compared to protocols without doxorubicin. Other options include single agent doxorubicin or a COP (cyclophosphamide, vincristine, prednisolone) protocol. Overall, remission rates range between 50-70%, with survivals around 6 months. However, some cats will have survival times >2 years. The following is a brief summary of different sites and prognoses.

* Multicentric: FeLV - cats with disease on one side of the diaphragm (median survival 17½ mos) do better than FeLV+ cats or cats with disease on both sides (median survival 3 months).
* GI: roughly 1/3 of cases respond to treatment, these cats live a median of 1 year.
• **Nasal**: very good prognosis – this disease is usually confined to the nasal cavity and can do excellently with local radiation, with median survival approx 1.5 years. If radiation not available, may respond to chemotherapy.

• **Mediastinal**: usually FeLV+, survival median 2-4 months.

• **CNS**: few reported cases, but overall poor survivals. To diagnose, 35% of cats had lymphoblasts in CSF. Close to 80% have bone marrow or renal involvement – testing these areas first in a paretic cat is a quicker and easier procedure. Chemotherapy is necessary, may need local treatment (surgery/radiation) also.

• **Renal**: median survival 3-6 months. Renal failure not a prognostic factor. 40% develop CNS involvement.

• **Ocular**: may be associated with systemic disease, but does occur as a primary, extra nodal site. These primary cases can have prolonged survivals with enucleation alone. Make sure to fully stage these cats in case there is systemic disease. FeLV+ and uveitis were poor prognostic factors. Median survival was not reached at 450 days of follow-up if FeLV- and no uveitis. With uveitis, 250 day median survival.

**Lymphocytic lymphoma**

Lymphocytic (a.k.a small cell or low grade alimentary) lymphoma most commonly occurs in the GI tract in cats. Because lymphocytic inflammatory bowel disease (IBD) is a major differential for small cell GI lymphoma, diagnosis requires full thickness (i.e. surgical) biopsies. It may be difficult to differentiate high-grade lymphocytic inflammatory bowel disease from lymphocytic lymphoma. Clonality testing via PCR or flow cytometry would be ideal, but the antibodies available to date do not allow for much confidence in the test results. One 2011 paper (J Comp Pathol, 2011 epub) reports that lymphoma is associated more with the T cell phenotype and fewer plasma cells than IBD. Treatment of lymphocytic lymphoma consists of chlorambucil (20 mg/m2 PO q14 days) and prednisolone (2 mg/kg PO q24 hours x 7 days, then 1.5 mg/kg PO q24 hours, then 1 mg/kg PO q24 hours, then 1 mg/kg PO q48 hours indefinitely). Chlorambucil, an alkylating agent, is extremely well tolerated. Initial monitoring includes a CBC before the first 4 treatments, then a CBC once every 2-3 months. Ideally, patients should be monitored for response to therapy with abdominal ultrasound. However, if the clinical signs of vomiting and diarrhea resolve, and the patient gains weight, remission may be assumed. Reported median survival times for cats with small cell GI lymphoma range from 700-900 days.