Description of clinical and pathological findings, treatment and outcome of feline large granular lymphocyte lymphoma (1996–2004)*

E. L. Krick¹, L. Little¹, R. Patel¹, F. S. Shofer¹, K. Sorenmo¹, C. A. Clifford² and J. L. Baez¹

¹Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania, Philadelphia, PA, USA
²Oncology Service, Red Bank Veterinary Hospital, Tinton Falls, NJ, USA

Abstract
Feline large granular lymphocyte (LGL) lymphoma is an uncommon, morphologically distinct variant of feline lymphoma. Limited information exists in the literature regarding pathological and immunohistochemical descriptions, clinical findings, treatment and survival times. The purpose of this study was to describe clinical features, treatment and outcome in feline LGL lymphoma. Medical records of 45 cats with LGL lymphoma were retrospectively evaluated. Decreased appetite/anorexia, weight loss, lethargy and vomiting were the most commonly reported clinical signs. All cats tested for feline leukaemia virus and feline immunodeficiency virus infection were negative. The mesenteric lymph nodes and small intestine were the most commonly affected organs. One complete response and six partial responses were noted in the 23 cats that received chemotherapy as their initial treatment. Median survival time for cats that were treated was 57 days. Based on these results, feline LGL lymphoma appears to be minimally responsive to chemotherapy and is associated with a grave prognosis.

Keywords
cat, chemotherapy, large granular lymphocyte, lymphoma

Introduction
Feline large granular lymphocyte (LGL) lymphoma is a morphologically distinct type of lymphoma that has been uncommonly described in the literature. The characteristic cytological or histopathological finding is the presence of multiple cytoplasmic azurophilic granules, which can vary in number and size between cats and within an individual cat.¹² LGLs have been documented in the peripheral blood of normal cats, constituting up to 13% of white blood cells.³ Feline LGLs have been determined to be of cytotoxic T cell or natural killer cell origin based on immunohistochemical staining and positive perforin-like immunoreactivity.¹³–⁵ In a recent report, cells from a majority of patients were found to be T cells (CD3+) that expressed CD8αα and CD103, which is consistent with the phenotype of feline and human intestinal intra-epithelial lymphocytes.⁶

Although very limited clinical information about feline LGL lymphoma is available, some consistent findings have been reported. Anorexia, vomiting and lethargy are the most commonly reported clinical signs, while a palpable abdominal mass is consistently reported as a common physical exam finding.²⁴–⁶¹ Feline LGL lymphoma does not appear to be associated with feline leukaemia virus (FeLV) infection, as few affected cats have tested positive for it.¹²⁴–⁶¹ Although there are no consistent haematological or serum chemistry

*Data presented in part at the 24th Annual Conference of the Veterinary Cancer Society, Kansas City, MO, USA, 3–6 November 2004.
abnormalities associated with feline LGL lymphoma, neutrophilia, increased peripheral LGLs and elevated total bilirubin, alanine aminotransferase and aspartate aminotransferase have been described.\textsuperscript{2,6,11} The most commonly affected anatomic locations include the gastrointestinal tract, abdominal lymph nodes, mesentry and liver, and elevated peripheral LGLs with or without bone marrow infiltration have been reported as well.\textsuperscript{1–4,6–11}

Although the phenotype of the cells and clinical aspects of feline LGL lymphoma have been described, little information regarding treatment protocols, response to treatment or survival time is available. The purpose of this study was to describe the clinical and pathological features of feline LGL lymphoma with an emphasis on evaluating response to treatment and outcome.

**Methods**

Cats diagnosed with lymphoma from January 1996 to December 2004 were identified via a computer search of biopsy and cytology records in the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania (MJR-VHUP) database and of the medical records database of Red Bank Veterinary Hospital. A review of histopathology and cytology reports by the first author and a clinical pathologist (L. L.) was performed to identify cats that fit the inclusion criteria of having a diagnosis of LGL lymphoma or lymphoma with the majority of lymphoblasts containing intracytoplasmic azurophilic granules. Cytology slides of included cases were reviewed by a clinical pathologist (L. L.) when available (41 of 45 cases), and cases were excluded if the review of samples indicated a diagnosis other than LGL lymphoma. Slides of affected bone marrow specimens were reviewed by two clinical pathologists (L. L. and R. P.). Signalment, historical and physical exam findings, laboratory test results, radiographic and ultrasonographic examination results, type(s) of treatment and response, disease-free interval, survival time and cytological and/or histopathological findings were recorded. Follow-up information was obtained from medical records and phone conversations with referring veterinarians. Animals that were lost to follow-up were censored at the date at which they were last known to be alive.

Response to treatment was subjectively categorized as: complete response, no clinical or gross evidence of disease; partial response, decrease in tumour burden of greater than 50% but less than 100%; stable disease, decrease in tumour burden of less than 50% or increase in tumour burden of less than 25%; and progressive disease, increase in tumour burden of greater than 25% or development of new tumours. Cats were classified into response groups based on physical examination findings and clinical signs of disease. Any response to treatment was required to last a minimum of 14 days. Response duration was determined for cats with a complete or partial response to treatment and was defined as the time between the initiation of treatment and the date at which progressive disease occurred. Survival time was defined as time from diagnosis to time of death or euthanasia and was analysed using Kaplan–Meier survival curves. Cats lost to follow-up or alive at the end of the study were censored at the time of last contact.

For the cats that received treatment, categorical patient factors evaluated to determine their prognostic value included presence of granulated lymphoblasts in the peripheral blood or bone marrow, neutrophilia, anaemia, increased serum bilirubin, decreased serum albumin and bicavitary (thorax and abdomen) involvement of LGL lymphoma. Body weight was another factor evaluated for its prognostic significance, and because it is a continuous variable, the median body weight was calculated, and cats with body weights above and below the median were compared. Curves for survival times were generated using the Kaplan–Meier product limit method. Differences in survival between groups were tested using the log rank test. \( P<0.05 \) was considered statistically significant. All data were analysed using SAS statistical software (Version 9.1, SAS Institute, Cary, NC, USA).

**Results**

Lymphoma was diagnosed in 594 cats at the MJR-VHUP during the study period, 43 of which were LGL lymphoma, according to the original cytology
or histopathology reports. Two additional cats from Red Bank Veterinary Hospital were included in the study, for a total of 45 cats. Slides from 41 cats were available for review, and no cat was excluded from the study after review of the slides. Breeds represented included domestic short hair ($n = 36$), domestic long hair ($n = 4$), Maine coon ($n = 3$), Persian ($n = 1$) and Siamese ($n = 1$). There were 23 males and 22 females, all of which were neutered. Median age was 10.8 years with a range of 2.1–16.8 years. Median body weight was 3.9 kg with a range of 2.4–7.8 kg. Presenting complaints are listed in Table 1. Abdominal mass ($n = 22$) and thin body condition ($n = 20$) were the most common physical exam abnormalities noted. Other examination findings included increased respiratory rate ($n = 11$), increased temperature ($n = 8$) and decreased bronchovesicular sounds ($n = 1$).

Staging tests included FeLV and feline immunodeficiency virus (FIV) (FeLV, $n = 28$; FIV, $n = 26$) testing (Petcheck FIV antibody and FeLV antigen detection kit; Idexx Laboratories, Westbrook, ME, USA, when performed at MJR-VHUP), complete blood count ($n = 43$), chemistry panel ($n = 42$), urinalysis ($n = 21$), chest radiographs ($n = 36$), abdominal ultrasound ($n = 39$) and bone marrow aspiration ($n = 17$).

All cats tested for FeLV ($n = 28$) and FIV ($n = 26$) infection were negative. Twenty-six cats were anaemic with a mean haematocrit of 24.5% (range 14.1–30.9%, reference range 31.7–48.0%). Neutrophilic leucocytosis was noted in 14 cats, and mean white blood cell and neutrophil counts for those 14 cats were 43,064 cells/µL (range 19,700–208,000 cells/µL, reference range 4,000–18,700 cells/µL) and 22,814 cells/µL (range 14,500–28,000 cells/µL, reference range 2,300–14,000 cells/µL), respectively. Four of these patients had neutrophilia with a regenerative left shift. Peripheral lymphoblasts were noted in four cats with a range of rare to 166,000 lymphoblasts/µL. Twelve cats were lymphopaenic with a mean lymphocyte count for those 12 cats of 475 cells/µL (range 100–700 cells/µL, reference range 800–6,100 cells/µL). One cat had a mature non-granulated lymphocytosis of 16,600 cells/µL. A marked eosinophilia of 42,500 cells/µL was noted in one cat. Thrombocytopenia was noted in eight cats (mean 155,500 platelets/µL, range 65,700–173,000 platelets/µL, reference range 175,000–500,000 platelets/µL), and thrombocytosis was noted in five cats (mean 776,200 platelets/µL, range, 568,000–1,227,000 platelets/µL).

The most common serum chemistry abnormality was elevated γ-glutamyltransferase activity ($n = 18$; mean 20 U/L, range 9–63 U/L, reference range 5–19 U/L). Other common serum chemistry abnormalities included elevated alkaline phosphatase activity ($n = 14$; mean 398 U/L, range 91–1,080 U/L, reference range 22–87 U/L), hyperbilirubinaemia ($n = 12$; mean 3.8 mg/dL, range 1.0–16.6 mg/dL, reference range 0.1–0.8 mg/dL), hypoalbuminaemia ($n = 10$; mean 1.9 g/dL, range 1.5–2.3 g/dL, reference range 2.4–3.8 g/dL) and elevated alanine aminotransferase activity ($n = 10$; mean 467 U/L, range 158–1,129 U/L, reference range 33–152 U/L). Azotaemia characterized by increased blood urea nitrogen or creatinine, or both, was noted in nine cats. Hyperglobulinaemia of 5.8 g/dL (reference range 3.1–5.0 g/dL) was noted in one cat. Serum electrophoresis was not performed in this patient.

Two of the azotaemic cats were diagnosed with renal failure based on isosthenuric urine. One of these cats had renal LGL lymphoma, while LGL lymphoma was not confirmed to involve the kidney in the other cat. Haematuria (ranging from 1–4

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased appetite/anorexia</td>
<td>35 (77.8)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>29 (64.4)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>25 (55.6)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>24 (53.3)</td>
</tr>
<tr>
<td>Palpable abdominal mass</td>
<td>11 (24.4)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>10 (22.2)</td>
</tr>
<tr>
<td>Weakness</td>
<td>7 (15.6)</td>
</tr>
<tr>
<td>Increased thirst</td>
<td>6 (13.3)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>5 (11.1)</td>
</tr>
<tr>
<td>Decreased thirst</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Icterus</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Neurological signs</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Lower urinary tract signs</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Sneezing</td>
<td>1 (2.2)</td>
</tr>
</tbody>
</table>
Clinical features and outcome of feline large granular lymphoma

...to too numerous to count red blood cells per high power field) was noted in four cats, and pyuria was noted in two of these cats. Four cats had bilirubinuria with concurrent hyperbilirubinemia, while three had bilirubinuria with normal serum bilirubin levels. Proteinuria was noted in 10 cats (six with concurrent haematuria) with isothenuria, nine of which underwent cystocentesis for urine collection. Because of the retrospective nature of the study, it was not possible to determine if urine was collected before or after intravenous fluid therapy.

Chest radiographs were performed in 36 cats. Abnormalities described on chest radiographs included pleural effusion \((n = 10)\), pulmonary parenchymal disease \((n = 7)\), mediastinal mass \((n = 6)\) and lymphadenopathy \((n = 6)\). Results of abdominal ultrasound examination were available for 39 cats, and all revealed at least one abnormality. Common abnormalities noted included a mass or thickening in the gastrointestinal tract \((n = 28)\), abdominal lymphadenopathy \((n = 24)\), peritoneal effusion \((n = 16)\) and abdominal mass of unknown origin \((n = 6)\). Other abnormalities consistent with lymphoma were noted in the following organs: kidney \((n = 8)\), spleen \((n = 11)\), liver \((n = 10)\) and pancreas \((n = 3)\). Bone marrow aspiration was performed in 17 cats, and granulated lymphoma infiltration was documented in eight cats. Granulated lymphoblasts comprised 1–30% of all nucleated cells in submitted bone marrow aspirates with a mean of 11.9% of all nucleated cells. Relative erythroid hypoplasia was frequently noted with five specimens exhibiting mild to moderate haemosiderosis.

Thirty-seven cats were diagnosed with LGL lymphoma by cytology, three via histopathology and five by both cytology and histopathology. More than one anatomic location was affected in 30 cats. The mesenteric lymph node(s) \((n = 20)\), small intestine \((n = 15)\) and liver \((n = 14)\) were the most commonly affected organs, followed by bone marrow \((n = 8)\), spleen \((n = 3)\), pancreas \((n = 1)\), kidney \((n = 1)\), eyelid \((n = 1)\) and peripheral blood \((n = 1)\). Pleural effusions from 11 cats and peritoneal effusions from eight cats were evaluated cytologically, and all were found to contain LGL lymphoma. LGL lymphoma was noted in both the pleural and the peritoneal effusions of two cats. Three cats had an abdominal mass of unknown origin, one had a perirenal mass, and one had a cranial mediastinal mass, all of which were diagnosed as LGL lymphoma.

Cytological preparations made from affected organs were of moderate to high cellularity and consistently contained moderate numbers of granulated lymphoblasts, few inflammatory leucocytes and scant normal tissue elements. Lymphoblasts were described as 12–20 μm in diameter with a round, clefted or cerebriform nucleus, variably distinct nucleoli, finely granular to lacy chromatin and a moderate amount of basophilic granular cytoplasm that was occasionally vacuolated. The cytoplasmic granules were magenta or azurophilic in colour, located in a focal paranuclear aggregate and punctate to globular in morphology, ranging from 2–4 μm in diameter (Fig. 1). Regardless of tissue of origin, neutrophils were often observed in increased frequency with few small lymphocytes and rare plasma cells. A coinciding eosinophilic infiltrate was present in one lymph node specimen and five gastrointestinal masses. Peritoneal and pleural fluid nucleated cell counts ranged from 1300 to 48900 cells/μm with 5–92% granulated lymphoblasts. Histopathologically, lymphoblasts had large round to ovoid nuclei, dispersed finely stippled chromatin and a single large prominent basophilic nucleolus. Cells displayed a scant amount of light...
basophilic cytoplasm that contained small eosinophilic granules.

Twenty-six cats in the study received treatment, including combination chemotherapy alone ($n=21$), chemotherapy followed by orthovoltage radiation therapy ($n=1$), chemotherapy followed by surgery ($n=1$), surgery alone ($n=1$) and surgery followed by chemotherapy ($n=2$). All cats treated with surgery had resection of intestinal masses. Four cats that received single-agent prednisone, one cat that received prednisone and lomustine and one cat that received prednisone and cyclophosphamide did not receive standard of care treatment for lymphoma in our clinic and were thus included in the untreated group. Induction chemotherapy consisted of a COP-based protocol (Table 2) in 20 cats and a CHOP-based protocol (one received mitoxantrone at 6.5 mg/m² instead of doxorubicin) in four cats. For the cats that received a CHOP-based protocol, two cats received the University of Madison–Wisconsin protocol, one received mitoxantrone as part of an intensified COP-based protocol and one received doxorubicin as part of an intensified COP-based protocol (Table 2). The dose of doxorubicin used was 1 mg/kg. One treatment delay occurred, and 7 dose reductions in five cats were recorded. Nine cats received rescue therapy consisting of chemotherapy ($n=9$) or chemotherapy and orthovoltage radiation therapy ($n=1$) after experiencing stable disease for 14 days ($n=1$) or progressive disease ($n=8$). The cat that received orthovoltage radiation therapy received one dose of 5 Gy and was euthanized before the course was completed. Five cats received one rescue protocol, two cats received two rescue protocols and two cats received three rescue protocols. Rescue protocols consisted of doxorubicin ($n=4$), an intensified COP-based protocol ($n=2$), lomustine and cytosine arabinoside ($n=2$), an intensified COP-based protocol and cytosine arabinoside ($n=1$), an intensified COP-based protocol and lomustine ($n=1$), lomustine ($n=2$), doxorubicin and carboplatin ($n=1$), MOPP ($n=1$), mitoxantrone ($n=1$) and methotrexate and L-asparaginase ($n=1$).

One complete remission and six partial remissions were noted in response to combination chemotherapy treatment, for an overall response rate of 30%. No responses to single-agent prednisone were documented. The cat that had a complete remission received a COP-based protocol, while two of the cats that experienced partial remissions received doxorubicin as part of their induction chemotherapy protocol. The duration of the complete remission was 17 days. One of the cats with a partial remission underwent surgical mass removal 30 days after the initiation of chemotherapy, and the other five cats experienced partial remissions of 14, 17, 19, 36 and 42 days. Five cats had progressive disease with chemotherapy, and two cats had stable disease for 14 and 68 days. One cat treated with surgery alone had disease progression after 91 days. One cat treated with surgery and chemotherapy did not have documented recurrence but was lost to follow-up at 62 days, while the two remaining cats treated with surgery and chemotherapy experienced progressive disease at 34 and 126 days. Fourteen cats were lost to follow-up or euthanized before response to treatment could be evaluated.

Median survival time for all cats was 20 days with a range of 0–288 days. Median survival time for treated cats, including surgery, orthovoltage radiation therapy or combination chemotherapy, was 57 days with a range of 0–267 days. Median survival time for untreated cats was 2 days with a range of 0–288 days. The difference in survival time between the two groups was statistically significant ($P=0.004$). The cat that lived the longest, with a median survival of 288 days, received prednisone

---

**Table 2.** Weekly sequential COP-based chemotherapy protocol used to treat feline lymphoma at the Veterinary Hospital of the University of Pennsylvania. After week 10, L-asparaginase is discontinued. Treatments are given weekly for 6 months, biweekly for 6 months, then every 3 weeks for 6 months. Prednisone is continued for the duration of the chemotherapy protocol, but the initial dose may be decreased over time. When intensified, vincristine and cyclophosphamide are given together once a week.

<table>
<thead>
<tr>
<th>Week 1</th>
<th>L-asparaginase</th>
<th>400 IU/kg SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 2</td>
<td>Vincristine</td>
<td>0.5 mg/m² IV</td>
</tr>
<tr>
<td>Week 3</td>
<td>Cyclophosphamide</td>
<td>100 mg/m² for 2 days (25 mg PO for 2 days)</td>
</tr>
<tr>
<td>Week 4</td>
<td>Vincristine</td>
<td>0.5 mg/m² IV</td>
</tr>
<tr>
<td>Week 5</td>
<td>Methotrexate</td>
<td>2.5 mg PO</td>
</tr>
</tbody>
</table>

IV, intravenously; PO, orally; SC, subcutaneously.
and cyclophosphamide and experienced progressive disease. For cats treated with combination chemotherapy, median survival time was 45 days. One cat treated with surgery alone survived for 92 days. Three cats were treated with surgery and chemotherapy; one with a survival time of 87 days, and the other two were lost to follow-up at 62 and 149 days. Seven cats responded to chemotherapy alone with a median survival time of 76.5 days versus 20 days for cats that did not respond to chemotherapy (n = 8; Fig. 2). The difference between these two groups was not statistically significant.

Thirty-one cats died or were euthanized for tumour-related reasons, while one cat was euthanized because of the development of myeloproliferative disease based on complete blood count and bone marrow aspirate results. Thirteen cats were lost to follow-up. Postmortem examination was performed on four cats. LGL lymphoma was documented in three cases based on cell morphology (n = 2) and/or positive phosphotungstic acid hematoxylin (PTAH) staining (n = 1) of the granules. The remaining cats had evidence of lymphoma on necropsy, but PTAH staining was not performed. Organs infiltrated with lymphoma on necropsy included small intestine (n = 4), mesenteric lymph nodes (n = 3), liver (n = 3), colon (n = 1), bone marrow (n = 1), sternal lymph node (n = 1), spleen (n = 1), pancreas (n = 1), kidney (n = 1), nasal cavity (n = 1), choroid (n = 1) and eyelid (n = 1).

Of the potential prognostic factors evaluated, bicavitary location of LGL lymphoma and decreased serum albumin were the only statistically significant factors found (Table 3). Cats with bicavitary involvement had a median survival time of 10 days versus 59 days for cats without it (P = 0.003). Cats with decreased serum albumin had a median survival time of 14.5 days, while cats with normal serum albumin had a median survival time of 67 days (P = 0.012).

Discussion

Feline LGL lymphoma is a malignancy for which there is limited published information, particularly in regards to treatment and outcome. This study provides the largest case series on feline LGL lymphoma and, as such, offers useful information regarding the clinical presentation and outcome in cats diagnosed with this variant of lymphoma.

The results from this study suggest that feline LGL lymphoma is an aggressive disease with a poor prognosis that is only minimally responsive to standard lymphoma chemotherapy protocols. Similar to previous studies, the most common anatomic locations affected included the mesenteric lymph nodes, gastrointestinal tract and liver. 1–4,6–10 None of the cats in the present study tested positive for FeLV infection, a finding that has been previously reported. 1,2,4,7,9 Because the number of cases of feline lymphoma associated with FeLV infection have decreased in general, however, this finding may not be specific to LGL lymphoma.13 The clinical presentation, outcome, low response rate and lack of durable response to treatment reported in this study are similar to those reported by most authors, 2,6–9,11 though prolonged survival times after surgical or medical treatment with chemotherapy have been described.7,8

The clinicopathological findings in our study population were non-specific and likely associated with LGL lymphoma infiltrate, systemic illness or an inflammatory response to tumour. Elevated cholestatic liver enzymes (specifically γ-glutamyltransferase and alkaline phosphatase) and hyperbilirubinemaia were the most commonly seen
serum chemistry abnormalities in this population of cats, and they were associated with hepatic LGL lymphoma in 13, eight and six cats, respectively. Hyperbilirubinaemia with elevations in alanine aminotransferase and/or aspartate aminotransferase, not \( \gamma \)-glutamyltransferase or alkaline phosphatase, has been previously reported in feline LGL lymphoma.\(^2,6\) Other potential causes of the liver enzyme elevations include cholangiohepatitis, hepatic lipidosis and post-hepatic cholestasis, but no evidence of these diseases was found in cats in this study. Anaemia and neutrophilia were the most common haematological abnormalities. Neutrophilia has been associated with other forms of lymphoma, and it is interesting to note that neutrophilia has been specifically associated with feline LGL lymphoma and may represent a paraneoplastic syndrome.\(^2,6,10,14\) The presence of neutrophilic inflammation in tumour samples found in this study in addition to peripheral neutrophilia may indicate both a local and a systemic inflammatory response to the tumour.

Staging results confirm that LGL lymphoma has a similar organ/tissue distribution to more common forms of feline lymphoma with the abdominal organs being most commonly affected. Neither the clinicopathological findings nor the anatomic distribution of lesions was found to be pathognomonic for LGL lymphoma. Cytology, histopathology or immunohistochemical staining is necessary to differentiate this form of lymphoma from non-LGL lymphoma.

From our data, chemotherapy combined with surgical resection of a primary intestinal mass in a cat with LGL lymphoma may result in an improved outcome compared with untreated cats. However, the median survival in cats that did not receive treatment was only 2 days, suggesting that they were euthanized shortly after diagnosis. This finding underscores the difficulty with assessing the effectiveness of a treatment by comparing survival times. Owners who decide to pursue treatment might be more likely to keep their cats alive longer than those owners who decide not to pursue further treatment. The benefit from chemotherapy in cats with LGL lymphoma is further debatable since there was no significant difference in survival between chemotherapy responders and non-responders with a median survival of 76.5 and 20 days, respectively. None of the cats in this study had survival times longer than 10 months, which is clearly less than noted with other types of lymphoma, where up to 35% of patients are long-term survivors.\(^1\)

Canine LGL lymphoma has been rarely described, and several distinct differences occur in this disease between these two species. LGL leukaemia and lymphocytosis are the most common forms described in the dog. Although there are some reports of dogs that are euthanized shortly after being diagnosed, the majority of cases in the literature have survival times of 6 months to over 3 years, as opposed to the outcome for cats found in the current study.\(^15–19\) When the cell type of origin has been determined, it is most commonly reported to be cytotoxic T lymphocytes.\(^15,17,18\) Canine LGL lymphocytosis has been reported in association with \textit{Ehrlichia} infection.\(^20\)
Proliferative diseases of LGLs in humans often follow one of two distinct clinical courses depending on whether the cause is cytotoxic T cell or natural killer cell lymphoma or leukaemia. Cytotoxic T cell lymphoma is frequently described as having a slowly progressive clinical course with treatment generally required only when the disease causes clinical signs or a significant decrease in other cell lines, such as neutropenia or anaemia. In contrast, natural killer cell leukaemia is characterized as an aggressive disease that is resistant to most chemotherapy protocols, which results in a poor prognosis.

Of the clinicopathological findings evaluated for prognostic significance in this study, only bicavitory disease location and hypoalbuminemia were found to be negative prognostic factors. Cats with disease involving the thoracic and abdominal cavities likely have very advanced disease, and decreased serum albumin may correlate with the severity of hepatic or gastrointestinal involvement. The clinical significance of these findings is unclear, however, as the median survival time of treated cats in this study is short. A diagnosis of LGL lymphoma versus another form of lymphoma appears to be a clinically important prognostic factor.

Weaknesses of this study include the small number of cats and its retrospective nature, which limit data interpretation and prevent standardization of treatment protocols. All the cats in this study were patients at a referral hospital, which could have resulted in a skewed population of cats with LGL lymphoma, as, generally, patients referred to a specialty hospital are likely to be more ill than those treated in general practice. It is possible that our hospital population is not representative of all cats with LGL lymphoma, and perhaps if a more general population were evaluated, the outcome data would be different. In addition, cytology or histopathology was not performed on every grossly abnormal organ in each cat, so the anatomic distribution of LGL lymphoma in this study is likely under-reported. Because so few cats responded to chemotherapy and half of the cats that had surgery were lost to follow-up, our study focused on survival time as opposed to remission duration. Larger studies may uncover more cats that respond to treatment, making remission duration more feasible to evaluate. The lack of significant difference in the survival times between responders and non-responders could be because of type II error because of the small number of cats that received chemotherapy, but the overall survival time for cats that received any type of treatment remains low.

Results from this study suggest that feline LGL lymphoma is poorly responsive to treatment. It is often associated with local and systemic neutrophilic inflammation, and its anatomic distribution is similar to that of other forms of lymphoma.

Future directions in the study of this disease may include in vitro studies to evaluate sensitivity to various chemotherapeutic agents in order to better identify effective chemotherapeutic drugs for this form of lymphoma. In addition, prospective studies evaluating the efficacy of different chemotherapy protocols and the utility of surgery in the treatment of feline LGL lymphoma are needed.

Acknowledgments

The authors thank Dr Adrienne French for reviewing histopathological specimens for the study.

References


