Published in final edited form as:

Vet Comp Oncol. 2018 September ; 16(3): 337–343. doi:10.1111/vco.12384.

Clinical characteristics and outcome in dogs with small cell T-cell intestinal lymphoma

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Abstract

Small cell intestinal lymphoma has not been well characterized in dogs. The objective of this study was to describe clinical characteristics and outcome in dogs with small cell intestinal lymphoma. We hypothesized that affected dogs would have prolonged survival compared to high-grade GI lymphoma. Pathology records were searched for dogs with histologically confirmed small cell GI lymphoma. Seventeen dogs with confirmed small cell intestinal lymphoma were identified, and clinical and outcome data were retrospectively collected. Histopathology was reviewed by a board-certified pathologist, and tissue sections were subjected to immunophenotyping and molecular clonality assessment. All dogs had small cell, T-cell, lymphoma confirmed within various regions of small intestine, with 1 dog also having disease in abdominal lymph nodes. All dogs had clinical signs attributable to GI disease; diarrhea (n=13) was most common. Ultrasonographic abnormalities were present in 8 of 13 dogs with abnormal wall layering (n=7) and hyperechoic mucosal striations (n=7) representing the most common findings. In total, 14 dogs received some form of treatment. The median survival time (MST) for all dogs was 279 days and the MST for the 14 dogs that received any treatment was 628 days. Dogs with anemia and weight loss at presentation had significantly shorter survival times and dogs that received a combination of steroids and an alkylating agent had significantly longer survival times. Small cell, T-cell, intestinal lymphoma is a distinct disease process in dogs, and those undergoing treatment may experience prolonged survival.

Keywords

Alimentary; canine; clonality; indolent; low-grade

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This work was conducted at University of California, Davis Veterinary Medical Teaching Hospital, Davis, CA.

The authors disclose no conflict of interest.

INTRODUCTION

Lymphoma is the most common neoplasm to occur in the dog, and the gastrointestinal (GI) tract is the most frequently involved extranodal site(1,2). In the majority of cases of GI lymphoma, the GI tract appears to be the primary location of disease, with no evidence of disease outside of the abdominal cavity, however there are some cases in which GI lymphoma is an extension of multicentric disease(3). In the current literature, information related to clinical characteristics, treatment, and outcome of dogs with GI lymphoma is limited to high-grade disease(3–5), with few isolated cases of small cell GI lymphoma interspersed into these studies. Recently, the pathological findings associated with small cell GI lymphoma in dogs have been described, including the uncommon nature of the disease, however limited clinical, treatment, and outcome information was presented in these studies(6–10). More recently, twenty dogs with low-grade gastrointestinal lymphoma were described by Lane et al. A majority of dogs were treated with a combination of chlorambucil and prednisone, with a reported median survival time (MST) of 424 days. No factors were found to be associated with survival(11).

In cats, it is well established that small cell (low-grade) GI lymphoma and intermediate to large cell (high-grade) GI lymphoma are two distinct clinical entities. These two diseases have differing treatment recommendations and prognoses, highlighting the importance of differentiation(12–14). Dogs and cats with high-grade GI lymphoma experience a rapid clinical course, and are consequently treated with aggressive multi-agent injectable chemotherapy protocols in order to target the rapidly dividing nature of the neoplastic cells. Even with treatment, most dogs with high-grade GI lymphoma will die of their disease within 4 months of diagnosis(3–5). Cats with high-grade GI lymphoma also experience a rapid clinical course and, despite treatment with chemotherapy, only 1/3 of cats experience prolonged survivals(15). This is in contrast to the typical and well-described clinical course of feline patients with small cell GI lymphoma, which is generally protracted. Due to the more indolent nature of small cell GI lymphoma in cats, aggressive injectable chemotherapy agents are not usually necessary and signs can generally be managed with long-term oral prednisolone and oral chlorambucil. Reported response rates are as high as 100% with MST ranging from 600–900+ days for cats receiving a combination of prednisone and chlorambucil(12,16–18).

Differentiating inflammatory bowel disease and similar non-neoplastic conditions from small cell GI lymphoma in both dogs and cats poses a difficult task for pathologists, as they can look similar under routine hematoxylin-eosin (HE) stain. Immunohistochemistry (IHC) and molecular clonality are beneficial to aid in the diagnosis of small cell GI lymphoma once biopsy samples are obtained, in order to differentiate a clonal population of cells consistent with lymphoma from a polyclonal population of cells consistent with non-neoplastic conditions. Cats with small cell GI lymphoma most commonly have mucosal T-cell lymphoma, reported in 98% of cats in one study(18). The most commonly documented immunophenotype in dogs with GI lymphoma is T-cell, occurring in 63% of cases in two separate reports(3,4), although a vast majority of these cases were high-grade GI lymphoma. In the most recent publication by Lane et al, 95% of dogs had CD3 positive IHC, and the

35% of dogs who had PARR analysis reported has clonal results consistent with T-cell lymphoma.

The purpose of this study was to describe clinical characteristics and outcome in a cohort of dogs with small cell GI lymphoma confirmed with histopathology, immunophenotyping, and molecular clonality assessment. An additional aim was to examine possible prognostic factors that may predict outcome in this population of dogs.

MATERIALS & METHODS

The veterinary histopathology database at the University of California, Davis (UCD) Veterinary Medical Teaching Hospital was searched for cases of canine small cell intestinal lymphoma between January 2000 and January 2016. Diagnoses were made from endoscopic biopsies or full-thickness surgical biopsies. All medical records were reviewed, and data collected included signalment, body weight, body condition score (BCS), owner reported clinical signs at presentation, staging diagnostics (including abdominal ultrasound images which were all reviewed by single board-certified radiologist [ALZ]), treatment, and date of death. Lymph nodes were considered enlarged based on the opinion of ALZ using previously reported size guidelines(19–21). Classification for lymph node enlargement was binary (yes/no). Follow-up information was obtained by contact with referring veterinarians, clients, or both. To meet selection criteria, dogs required follow-up for at least one veterinary visit after diagnosis or until death.

All pathology samples were reviewed by a single board-certified pathologist (PFM), and criteria for diagnosis of small cell lymphoma was based on the presence of a predominantly small lymphocytic infiltrate, IHC with CD3 antibody to confirm T-cell phenotype, and molecular clonality assessment with polymerase chain reaction (PCR) as described previously(18,22). T-cell phenotype was established when the dominant lymphoid population in the lamina propria and epithelium were CD3 positive. B-cell IHC and clonality was planned in dogs that were not CD3 positive on IHC.

The Kaplan-Meier product limit method was used to estimate survival, which was defined as the date biopsies were obtained to the date of death from any cause, and the log-rank test was used to assess the effect of various factors on survival. Survival times were censored if dogs were alive at the study's end or lost to follow-up. Death was assumed to be related to lymphoma in all cases. Factors assessed for effect on survival include presenting complaints of diarrhea, vomiting, weight loss and presence of a low BCS (defined as <5 on a 9 point scale, with 5 being the ideal BCS(23)), anemia, hypocobalaminemia, hypoalbuminemia, effusion at the time of diagnosis, and treatment received. A P-value of <0.05 was considered statistically significant.

RESULTS

Seventeen dogs with small cell intestinal lymphoma met selection criteria. Two (12%) dogs underwent full-thickness biopsies during an abdominal exploratory procedure and 15 (88%) had partial-thickness biopsies obtained endoscopically.

Patient characteristics, owner reported presenting complaints, and physical examination findings are listed in table 1. The median age was 9 (range, 2–13 years) and the median body weight was 20.1 kilograms (range, 4.3–43 kilograms). The median BCS (on a 1–9 scale where 1 = emaciated, 5 = ideal, and 9=obese(23)) was 5 (range, 2–8). Clinical signs attributable to small cell intestinal lymphoma were present in all dogs.

A CBC from the time of diagnosis was available for 14 (82%) dogs. There were no abnormal findings on CBC in 6 (43%) dogs. The abnormal CBC findings are reported in Table 2. A biochemical panel from the time of diagnosis was available for 16 of 17 (94%) dogs. All evaluable dogs had at least one abnormal finding. The main biochemical abnormalities are reported in Table 3. Regarding the 11 (69%) dogs with hypoalbuminemia, this was considered mild in 2 (11%) dogs (albumin between 2.6–3.4 g/dL), moderate in 7 (44%) dogs (albumin between 1.6–2.5 g/dL), and severe in 2 (11%) dogs (albumin ≤1.5 g/dL). Serum cobalamin was evaluated in 14 of 17 (82%) dogs. A normal result was found in 4 (29%) dogs, while 10 (71%) dogs had documented hypocobalaminemia (cobalamin <272ng/L). Serum folate was available in 8 (44%) dogs. Three (37%) of these dogs had a high serum folate level (folate >18.6ng/mL), while 5 (63%) had a normal serum folate level (folate 6.5–18.6 ng/L).

Thoracic radiograph reports or images were available in 11 of 17 (65%) dogs. There was no evidence of pulmonary neoplasia on thoracic radiographs of any dog. Eight dogs (73%) were noted to have thoracic radiographs within normal limits, while 1 dog had cardiomegaly, pleural effusion, and bronchopneumonia, 1 dog had a pulmonary bronchointerstitial pattern, and 1 dog had focal heavy interstitial opacities of the right middle lung lobe consistent with aspiration pneumonia.

Abdominal ultrasonographic images were available for review in 13 of the 17 (76%) dogs, and 11 of these 13 (85%) dogs had lymph node measurements available. No abnormalities were present within the GI tract or surrounding mesenteric lymph nodes in 5 (38%) dogs, while 8 (61%) of dogs had abnormalities present. These included abnormal wall layering (n=7, 54%), hyperechoic mucosal striations (n=7, 54%), enlarged abdominal lymph nodes (n=6, 46%), fluid contents within the lumen (n=6, 46%), thickened muscularis propria (n=5, 38%), and effusion (n=5, 38%). Effusion was sampled in 3 of 5 dogs (60%), and was consistent with a transudate in all sampled. Abnormalities were present in all sections of the small intestinal tract in 3 (23%) dogs, and only within the duodenum and jejunum in 5 (38%) dogs. In dogs with enlarged abdominal lymph nodes, the median measurement was 0.6cm (range 0.579–1.08cm).

All dogs were confirmed to have small cell intestinal lymphoma on pathology review. The most salient features on routine HE were predominantly lymphocytic infiltrates within the intestinal villous lamina propria and epithelium. These infiltrates were often more pronounced in the villous tips. All lymphomas in the current study were CD3 positive, confirming T-cell immunophenotype. Deoxyribonucleic acid was available in all dogs for PCR analysis. Fifteen (88%) had a clonal rearrangement of T-cell receptor gamma (TRG) locus and two (12%) had a polyclonal rearrangement of the TRG locus. The specific location of biopsy collection was recorded in 13 (76%) cases, with the remaining 4 (24%)

cases only identifying the location of collection as “small intestine”. Within the 13 samples that recorded a specific site, 8 (61%) dogs had lymphoma confirmed in multiple locations. In total, 11 (85%) dogs had confirmed disease in the duodenum, 2 (15%) dogs had confirmed disease in the jejunum, 7 (54%) dogs had confirmed disease in the ileum, and 1 (8%) dog had confirmed disease in the ileocolic region. Additionally, there was 1 (6%) dog with confirmed disease in abdominal lymph nodes. There were no dogs with confirmed small cell lymphoma in the stomach or the colon. While 88% of dogs underwent endoscopy for biopsy procurement, 65% of dogs (n=11) had ileal samples obtained for histopathology.

Overall, 14 (82%) dogs underwent some form of therapy. Six (42%) patients were treated with corticosteroids alone. Eight (57%) dogs received a combination of steroids and an alkylating agent with 7 dogs receiving chlorambucil and 1 dog receiving cyclophosphamide and lomustine. One dog treated with corticosteroids alone and one dog treated with a combination of steroids and an alkylating agent received L-asparaginase at the beginning of their treatment protocol. Three (18%) dogs did not receive any treatment for their small cell intestinal lymphoma.

The MST for all patients was 279 days (range 6–1,079 days). The MST of dogs (n=14) that received any treatment was 628 days (range 12–1,079 days). Survival times for the 2 dogs with polyclonal PCR results were 6 and 7 days. Three dogs were still alive at the time of data accrual (range 490–764 days) and 1 dog was lost to follow up (12 days). These cases were censored from survival analysis at the time of last follow up, and the median time to follow up for censored dogs was 573 days (range 12–764 days). The results of prognostic factor assessment are listed in Table 4. Weight loss, anemia, and type of therapy received were significantly associated with outcome.

Of note, 2 of 17 (12%) patients were diagnosed with large cell lymphoma within their abdominal cavity 89 and 127 days after diagnosis of small cell intestinal lymphoma. One dog had received treatment with steroids, chlorambucil, and L-asparaginase. This dog had a new abdominal mass noted on abdominal radiographs 127 days after his initial histopathology confirmed small cell intestinal lymphoma. Cytology was performed of the abdominal mass which revealed large cell lymphoma. He continued treatment with prednisone and chlorambucil, and was euthanized 43 days later. The other dog was receiving treatment with steroids alone. This dog had a new finding of a moderately enlarged mesenteric lymph node measuring 1.3cm in thickness noted on abdominal ultrasound 89 days after her initial histopathology diagnosed small cell intestinal lymphoma. Cytology was performed of the enlarged mesenteric lymph node which revealed large cell lymphoma. The dog continued treatment with steroids alone and was euthanized 38 days later.

DISCUSSION

This study is the first to describe the clinical characteristics and outcome in dogs with histologically confirmed small cell intestinal lymphoma. Previous studies describing the disease entity have focused on pathologic, immunohistochemical, and molecular characteristics and did not include information describing clinical features(6,7,22). Based on results presented here, dogs with small cell intestinal lymphoma appear to have a favorable

outcome when undergoing any type of therapy, with an MST of 628 days. This is not entirely surprising, given that cats treated with a combination of steroids and alkylating agents (most typically chlorambucil) have MST >600 days(12,16–18), which is comparable to the MST in the current study. More specifically, dogs receiving a combination of steroids and an alkylating agent had a prolonged survival compared to dogs receiving no treatment or receiving treatment with steroids alone (P=0.002). Additionally, the MST in the current study is more favorable compared to historic reports of dogs with high-grade GI lymphoma, suggesting that it is, in fact, a separate disease entity(3–5).

Three factors in the current study were shown to significantly influence survival, including weight loss or anemia at the time of diagnosis which were present in 41% and 36% of dogs, respectively and the type of therapy received. Weight loss and anemia at the time of diagnosis have not been previously reported as prognostic factors in cats with small cell GI lymphoma or in dogs with high-grade GI lymphoma, however both a low body condition score at diagnosis and anemia have been reported as overall negative prognostic indicators in dogs with lymphoma(24,25). Dogs that were underweight at the time of diagnosis of lymphoma were reported to have a lower MST in Romano's study compared to dogs that had an ideal weight or were overweight(25). The presence of anemia at diagnosis has been correlated with a decreased survival in dogs with lymphoma, conferring a 2.37-fold higher likelihood of death in dogs with a packed cell volume <35%(24). Within the current study population, there are many possible explanations for the anemia present in 5 dogs, including anemia of inflammatory disease, iron deficiency anemia related to chronic GI hemorrhage, or production of anemia-inducing substance by tumor cells(26–28). The presence of weight loss at the time of diagnosis may be indicative of more severe infiltration of disease leading to malabsorption in those dogs, which may account for their worsened survival. Additionally, weight loss may contribute to concern for a worsened quality of life which may more readily prompt humane euthanasia. In the current study, there were 3 dogs that did not undergo any form of therapy which affected the overall MST reported (279 days), and was also significantly associated with a lower MST (P=0.002). The lack of treatment in these 3 dogs could have been, in part, due to a decreased awareness of this disease entity, resulting in a guarded prognosis being given to the owners based on previous reports of poor outcomes in dogs with high-grade GI lymphoma(3–5). Increasing awareness of the diagnosis of small cell intestinal lymphoma and associated survival times may allow oncologists to better advise owners of dogs diagnosed with this disease. No other factors assessed were associated with outcome in this cohort of dogs, however given the small number of dogs assessed, it is possible that, with further evaluation, additional factors may be found that correlate with outcome.

Dogs diagnosed with small cell intestinal lymphoma were generally middle aged or older, with one 2-year old dog present. Sixty-five percent of dogs in the current study were male. Interestingly, male dogs have been proposed to have a predilection for development of high-grade gastrointestinal lymphoma(5), and in the recent Lane et al publication, there was a 1.9:1 male:female ratio noted in dogs with low-grade gastrointestinal lymphoma(11), indicating that male dogs may truly have a higher risk of developing lymphoma of the intestinal tract. In all dogs, clinical signs were nonspecific and indistinguishable from those associated with non-neoplastic GI disease, which is similar to what has been reported in

previous studies(6–11). There were various hematologic and biochemical abnormalities found within the dogs in the current study, most of which can be explained by presence of infiltrative GI disease. Hypoalbuminemia was present in 69% of the dogs in the current study, and has been reported in up to 49% of cats with small cell GI lymphoma(29)although was not present in any cats within a separate study(17). Hypoalbuminemia was also reported in 50% of the recent Lane et al study(11). It is likely that the hypoalbuminemia present in dogs within the current study occurred primarily due to loss of low molecular weight proteins across a compromised intestinal wall(29). In the current study, hypoalbuminemia showed no statistical influence on survival, however further studies will be beneficial to help confirm this. Hypocobalaminemia was present in 71% of dogs evaluated in the current study, which is similar to the proportion of cats with small cell GI lymphoma (78%) presenting with hypocobalaminemia(16) and higher than Lane et al's recent report of dogs with low-grade gastrointestinal lymphoma(11). Cobalamin is absorbed exclusively in the ileum, as a complex of intrinsic factor and cobalamin, and is a cofactor in several important enzymatic reactions(30). Given the high percentage of hypocobalaminemic dogs in the current study, it would be useful to routinely measure this value in dogs with small cell intestinal lymphoma in order to understand the clinical implications and to initiate parenteral supplementation if necessary. This value could also be monitored throughout a treatment protocol, to ensure no changes in supplementation are necessary.

The reported ultrasonographic features of small cell intestinal lymphoma in cats include diffuse intestinal wall thickening (most specifically, a thickened muscularis propria) with or without preservation of wall layering and mesenteric lymph node enlargement(17,31). In the current study, these were also common findings in dogs. Two additional findings that have not been as commonly reported in cats with small cell intestinal lymphoma include hyperechoic mucosal striations and effusion, both of which are seen commonly in dogs with protein losing enteropathies, most specifically intestinal lymphangiectasia(32). It is proposed that the hyperechoic mucosal striations represent lacteal dilation(33) and this could be a primary finding with small cell intestinal lymphoma in dogs or represent concurrent lymphangiectasia that is separate from the lymphoma. The pleural and peritoneal effusion seen in 38% of dogs within the current study was an unexpected finding. The most likely explanation for the effusion found in these dogs is the presence of profound hypoalbuminemia, especially considering that the 3 dogs with sampled effusion was consistent with transudate. However, not all dogs with effusion had an albumin that was considered low enough to explain the presence of effusion. This suggests that other etiologies must be considered for effusion in these dogs, including the potential that it is related to malignancy. Importantly, study results suggest that an ultrasonographically normal GI tract should not preclude recommendation for intestinal biopsies in dogs with clinical signs of GI disease, as 5 dogs (38%) in the current study did not have any ultrasonographic changes to the GI tract. This has also been reported in 15% of cats with the same disease(34). Within the current study, the 5 dogs that had an ultrasonographically normal GI tract all either had significant clinical signs attributable to GI disease or hematologic and biochemical abnormalities consistent with GI disease (anemia, hypoalbuminemia, hypocobalaminemia) which lead to GI biopsies despite the lack of ultrasonographic findings.

Lymphoma was diagnosed in more than one region of the intestinal tract in at least 61% of the cases in the current study, which is similar to findings in cats where diffuse or multifocal disease is common(17). Given that a majority of dogs in the current study underwent endoscopy for biopsy procurement, it is likely that a higher percentage of dogs had more diffuse or multifocal disease distribution considering the limitations of endoscopic biopsies, including lack of full-thickness tissue sampling, inability to assess the entirety of the GI tract, especially the ileum which has been proposed as an important site of sampling in cats with intestinal lymphoma(35). It is possible that dogs with small cell intestinal lymphoma may have been overlooked diagnostically without the addition of ileal biopsies, however overall, 65% of dogs had biopsies from the ileum documented in the current study. Additionally, with the lack of full-thickness biopsies in a majority of dogs in the current study, if the lymphoma lesions were located deeper in the intestinal wall, they could have again been overlooked diagnostically. Interestingly, there was no small cell lymphoma confirmed in any of the sections of stomach or colon analyzed, however not every patient had these tissues biopsied. It is possible that small cell lymphoma within the GI tract of dogs is limited to the small intestinal tract, which has been proposed in cats given the particular trafficking pattern of T cells in the intestine(18,36). However, given the limited number of dogs analyzed in the current study, further evaluation into this disease may reveal cases with small cell gastric or colonic lymphoma.

In order to confirm the diagnosis of small cell intestinal lymphoma, IHC was used to show T-cell morphology for all cases. A clonal rearrangement of TRG was confirmed in 15 (88%) dogs diagnosed with small cell intestinal lymphoma, supporting the diagnosis of T-cell neoplasia when used in conjunction with pathology review and immunophenotyping. Lack of demonstration of a clonal population in 2 of 17 dogs in our study is consistent with the previously published sensitivity of this PCR-based assay(6,22). Based on careful histological review of morphology and immunophenotype results, the 2 polyclonal cases in this study could be interpreted as false-negative results. Given that severe infiltration of inflammatory lymphocytes concomitant with small cell intestinal lymphoma has been reported in cats with the same disease(17), this is the most likely cause of the false-negative result, leading to a decrease in the relative number of tumor cells present which may fall below the PCR detection limit(37,38). Other possible explanations for the 2 polyclonal results is unknown mutations in the variable (V) and joining (J) segments or lack of primer coverage of unknown V and J segments. Alternatively, this finding could suggest that the polyclonal cases were not representative of small cell intestinal lymphoma. It has previously been reported that dogs with protein losing enteropathies where a clonal population is demonstrated have a worsened overall prognosis than dogs with a polyclonal result(8–10), however the 2 dogs with polyclonal results in the current study had very poor survival times of 6 and 7 days respectively. Given the poor survival times in these dogs, despite having polyclonal results, it is likely that they were affected by severe clinical disease. Overall, it would be ideal to use a combination of histopathology, IHC, and PCR in all cases where a lymphocytic infiltrate is present within the intestinal tract in order to most accurately identify the proportion of these cases that truly represent small cell intestinal lymphoma. Once this combination is applied to clinical patients, it will allow for a better understanding of the most appropriate treatment recommendations.

Interestingly, 2 (12%) dogs in the current study had documentation of large cell lymphoma within the abdominal cavity at a later date after diagnosis of their small cell intestinal lymphoma. Cytology at the time of diagnosis of small cell lymphoma was not available, as this diagnosis was made histopathologically in both cases. Both of these dogs were undergoing treatment, one with corticosteroids and chlorambucil and the other with steroids alone. It is unknown if this represents true transformation of small cell intestinal lymphoma or de-novo high-grade lymphoma due to lack of confirmation with matched molecular clonality assessment. Future studies with a larger number of dogs with small cell intestinal lymphoma may allow a better understanding about whether true transformation to high-grade lymphoma exists.

Limitations of this study include low case numbers, inconsistent diagnostics and treatments, and its retrospective design which lead to inconsistent follow-up (one dog in the current study was lost to follow-up). Survival times may have been underestimated in some, because dogs were considered to be dead of small cell intestinal lymphoma in all cases, and many dogs were humanely euthanized which promotes a more subjective survival analysis. Lastly, as discussed above, the inconsistent method of biopsy procurement is another limitation that may have affected establishment of a diagnosis in some dogs. Future studies with more cases and more uniform treatments will help better define the clinical features of this disease, and allow for a better understanding of necessities for biopsy procurement.

In conclusion, the results of this study suggest that small cell intestinal lymphoma in dogs is a distinct clinical entity and, if treated, may carry a favorable prognosis. The diagnosis of small cell intestinal lymphoma can be challenging and ultimately requires histopathology with IHC and molecular clonality assessment for definitive confirmation. Further prospective trials will be beneficial to confirm the clinical characteristics and outcome information reported in the current study and to help elucidate the best recommended treatment for these dogs.

Acknowledgments

Funded by the Center for Companion Animal Health, University of California, Davis; Davis, CA.

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Table 1

Patient characteristics, owner reported presenting complaints, and physical examination findings in 17 dogs with small cell intestinal lymphoma

	n	%
Breed		
Boston terrier	2	12
Border collie	2	12
German shepherd dog	2	12
Mixed breed dog	2	12
Other pure breed dogs	9	53
Sex		
Male castrated	10	59
Male intact	5	29
Female spayed	1	6
Female intact	1	6
Owner reported presenting complaints		
Diarrhea	13	76
Weight loss	7	41
Inappetence	7	41
Vomiting	7	41
Lethargy	2	53
Labored breathing & distended abdomen	1	6
Labored breathing	1	6
Borborygmous	1	6
Physical exam abnormalities		
Muscle wasting	5	29
Distended abdomen	4	23
Thickened intestinal tract	2	12
Dull heart & lung sounds	1	6
Painful abdomen	1	6
Dehydration	1	6

Table 2

Complete blood count in 14 dogs with small cell intestinal lymphoma

CBC abnormality*	n	%
Hematocrit		
<40%	5	36
Reticulocytes		
≤65,000/μL	2	14
>65,000/μL	3	21
White blood cells		
>13,000/μL	4	29
Neutrophils		
Bands present	1	7
>10,500/μL	4	29
Monocytes		
>1,200/μL	2	14
Platelets		
>400,000	2	14

* Reference values for UCD laboratory

Table 3

Biochemical abnormalities in 16 dogs with small cell intestinal lymphoma

Biochemical abnormality*	n	%
Albumin		
≤3.4 g/dL	11	69
Calcium		
<9.6 mg/dL	11	69
>11.2 mg/dL	1	6
Globulin		
<1.7 g/dL	4	25
>3.1 g/dL	3	19
Cholesterol		
<139 mg/dL	9	56
Blood urea nitrogen		
<11 mg/dL	7	44
>33 mg/dL	5	31
Creatinine		
<0.8 mg/dL	9	56
>1.5 mg/dL	1	6

*Reference values for UCD laboratory

Table 4

Factors evaluated for effect on survival in dogs with small cell intestinal lymphoma

Factor evaluated	n	MST (days)	*P*-value
Diarrhea			0.80
Present	12	279	
Not present	5	127	
Vomiting			1.0
Present	7	279	
Not present	10	173	
Weight loss			0.03
Present	8	118.5	
Not present	9	636	
Anemia			0.01
Present	5	67	
Not present	9	636	
Hypocobalaminemia			0.30
Present	10	171.5	
Not present	4	Not reached	
Hypoalbuinemia			0.08
Present	11	170	
Not present	6	734	
Effusion			0.80
Present	5	127	
Not present	12	279	
Body condition score			0.30
≥5	9	636	
<5	8	170	
Treatment			0.002
None	3	7	
Steroids	6	127	
Steroids + alkylating agent	8	628	