FOCUS ON FELINE GASTROENTEROLOGY

Feline Friendly Article

The recent literature focus of feline gastroenterology is on small bowel disease, especially inflammatory bowel disease (IBD) and lymphoma.

- **Norsworthy and colleagues** documented that chronic small bowel disease (CSBD) is a cause of chronic vomiting, with or without weight loss, and outlined the process of diagnosis. The study also determined that CSBD is usually a segmental disease best diagnosed with full-thickness biopsies taken via laparotomy.
- **Daniaux and colleagues** looked at small bowel wall thickening, as documented by ultrasound, finding that the thickness of the muscularis propria in cats with IBD and lymphoma was about twice that of normal cats. However, there is no significant difference between the two diseases; therefore, ultrasound cannot reliably differentiate them.
- **Kiupel and colleagues** also examined how to differentiate between IBD and lymphoma and concluded that histopathology alone may not be sufficient. Immunohistochemistry (IHC) and polymerase chain reaction (PCR) for Antigen Receptor Rearrangement (PARR) increase diagnostic accuracy substantially, especially when performed on full-thickness biopsies of the small bowel wall.
- **Krick and colleagues** looked at predicting the outcome of chemotherapy for cats with lymphoma. They concluded that weight loss during the first 2 months of chemotherapy is a negative prognostic indicator.

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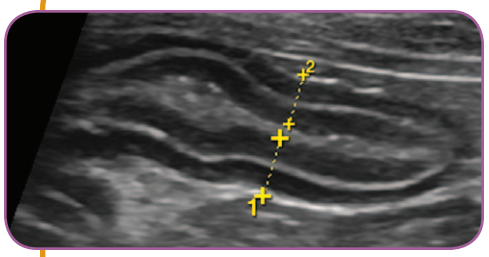


ULTRASONOGRAPHY OF THICKENED BOWELS

This prospective study of 32 cats compared healthy control cats (*n* = 19) to those with full thickness surgical biopsy diagnosis of small cell T-cell lymphoma (*n* = 7) or IBD (*n* = 6). Similar studies have evaluated muscularis propria thickening in cats with IBD and lymphoma, but this is the first study to specifically evaluate small cell T-cell lymphoma.

Diagnosis of IBD or small cell T-cell lymphoma was determined based on histology, immunohistochemistry, and PCR clonality for rearrangement of T-cell receptor gamma.

- Cats with lymphoma had histologically confirmed transmural disease.
- Cats with IBD had no disease beyond the mucosal layer, suggesting that yet undiscovered factors are at play.

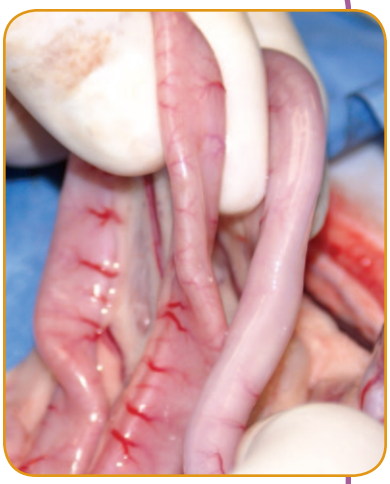
A minimum of 3 ultrasound images were collected from the duodenum, jejunum, and ileum in transverse and sagittal planes; ultrasonography revealed that:

- Bowel thickening (segmentally or diffusely) in cats with IBD and small cell T-cell lymphoma was related to increased muscularis propria, with preservation of wall layers but no mass formation.
- In the above cats, mean thickness of the muscularis propria was twice that of healthy cats.
- Regarding these measurements, there was no significant difference between cats with IBD compared to those with lymphoma.

Feline GI small cell T-cell lymphoma, which may have been previously underappreciated, is becoming recognized as a distinct form of GI lymphoma in cats, but appears similar to IBD on ultrasound and histology.

Daniaux LA, Laurenson MP, Marks SL, et al. Ultrasonographic thickening of the muscularis propria in feline small intestinal small cell T-cell lymphoma and inflammatory bowel disease. *J Fel Med Surg* 2014; 16(2):89-98.

CHRONIC VOMITING DIFFERENTIAL DIAGNOSIS



Chronic vomiting is so common in cats that their owners often do not consider it abnormal. It often occurs for years—as often as daily to weekly—but the cat seems normal otherwise. However, the authors consider **vomiting more than 2 times per month to be abnormal** and justification for further evaluation.

The authors studied 100 cats, ranging in age from 1 to 18 years. Of these cats, 26 were presented for wellness examinations and, in each case, the owner did not consider frequent vomiting a sign of illness. The remaining cats had chronic diarrhea and/or weight loss but, in some cases, neither vomiting nor diarrhea accompanied weight loss.

Cats with "abnormal" vomiting (≥ 2 times/month) or weight loss should be evaluated by ultrasound. Intestinal wall thickening on ultrasound was defined as 0.28 cm or greater in 2 or more segments, which was a consistent finding. The authors found that 76 cats had some bowel with normal ultrasound measurements and some with abnormal measurements; segmental disease was confirmed at surgery. Based on these findings, biopsies (from the liver, pancreas, and 3 or more full-thickness biopsies from the small bowel) were performed in 100 cats.

Each cat's tissues were tested with IHC staining and the ambiguous cases had PCR for PARR testing:

- Only 1 cat had normal results
- 49 had chronic enteritis, and were as old as 16 years
- 50 had neoplasia; 46 of these cats had lymphoma and were as young as 8 years.

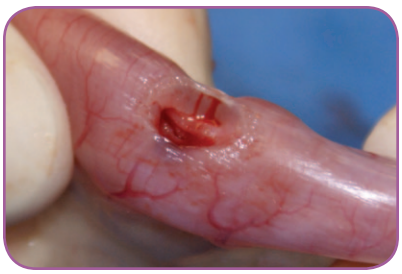
This leads to the conclusion that CSBD is an important differential for weight loss, even if gastrointestinal (GI) signs are *not* present.

In general, younger cats were more likely to have chronic enteritis, while the older cats typically had lymphoma. However, there was significant overlap in ages of the 2 groups. This data supports the belief that, in some cats, chronic enteritis can transition to lymphoma.

Of the cats with lymphoma, 85% had T-cell or small cell lymphoma, which is in contrast to earlier studies that determined B-cell or large cell lymphoma was predominant. This finding likely reflects the difference in early versus late diagnosis of the disease; it also may reflect detection of a more covert form of lymphoma that, without histopathology guidelines, IHC, and PARR, may have been previously misdiagnosed as IBD.

A wellness examination is a valuable screening tool for chronic small bowel disease, but the veterinarian or technician must be proactive - Ask about vomiting and its frequency.

Norsworthy GD, Estep JS, Kiupel M, et al. Diagnosis of chronic small bowel disease in cats: 100 cases: 2008-2012. *JAVMA* 2013; 243(10):1455-1461.



DIFFERENTIATING IBD FROM LYMPHOMA

Correct diagnosis and differentiation between IBD and lymphoma is important for proper treatment and prognosis. However, pathologists can face a daunting to impossible challenge differentiating these 2 diseases based on histomorphology alone.

B-cell lymphomas have a distinct, fairly identifiable cellular morphology which, in the past, may have selectively increased diagnostic yield for these tumor types. Now we appreciate that most primary feline intestinal lymphomas are of T-cell origin.

T-cell lymphomas and IBD are both characterized by small lymphocyte infiltration, with neoplastic cells often invading beyond the mucosa.

This retrospective study examined 63 cats with histologic diagnosis of IBD or lymphoma. Samples were collected via full thickness surgical biopsy (n = 50) or endoscopy (n = 13). To evaluate the validity of these purely histologic diagnoses,

Biopsy sample quality is paramount to accurate diagnosis; full thickness surgical biopsy specimens are preferred to allow evaluation of lymphocyte invasion depth—a major criterion with regard to differentiation of IBD from lymphoma.

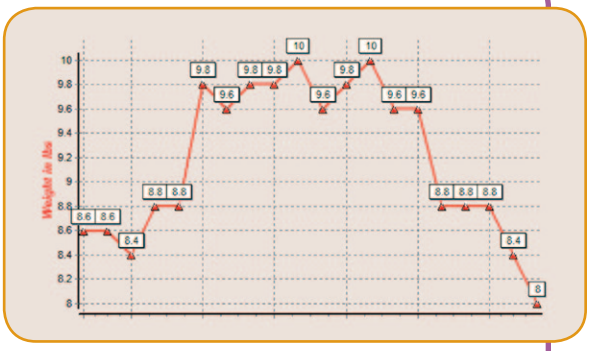
samples were evaluated by IHC and PCR. Based on the results of these tests:

- Of cases originally diagnosed as IBD by histopathologic examination alone, 53% were reclassified as T-cell lymphoma when IHC and PCR results were evaluated in conjunction with hemotoxylin and eosin (HE) stained sections.
- Of cases originally diagnosed as T-cell lymphoma by histopathologic examination alone, 8% were reclassified as IBD when IHC and PCR results were evaluated in conjunction with HE findings.

These findings suggest that histopathology alone cannot differentiate IBD and small cell lymphoma, leading to misdiagnosis. However, IHC and PCR—combined with histopathology—are likely to markedly increase diagnostic accuracy.

Kiupel M, SMedley RC, Pfent C, et al. Diagnostic algorithm to differentiate lymphoma from inflammation in feline small intestinal biopsy samples. *Vet Path* 2011; 48:212-222.

BODY WEIGHT'S ROLE IN LYMPHOMA



Lymphoma is the most common hematopoietic tumor in cats. This retrospective study determined whether weight changes in 209 cats with lymphoma correlated to specific survival time during treatment. Lymphoma had been confirmed by cytology or histopathology, and chemotherapy was pursued, with appropriate follow-up at 1, 2, 3, and 6 months (± 10-day window).

Three categories were created: Cats that (1) gained weight (> 5% increase), (2) maintained weight, or (3) lost weight (> 5% decrease). Results demonstrated that:

- Baseline body weight (prior to commencement of chemotherapy) was not prognostic for survival.
- In cats with large cell lymphoma, those that had gained or had stable weight at the 1-month time point had significantly longer survival than those that had lost weight.
- Cats with small cell lymphoma demonstrated no statistical prognostic significance in weight change; however, a clinically (but not statistically) significant negative prognostic difference was identified at the 2-month time point.
- The authors speculated that the lack of statistical prognostic significance may be due to more indolent behavior and slow progression associated with small cell lymphoma, and weight changes—at these thresholds and timeframes—may not have been appreciated.
- During treatment, small cats cats (< 3 kg), tended to gain weight while larger cats (≥ 3 kg) lost weight.
- Neither anatomic location of lymphoma (GI versus non-GI) nor cell type (large cell versus small cell) affected weight changes.

The authors noted several limitations of the study, largely due to its retrospective nature: hydration status was not included, body condition scores were not consistently available, and small cell lymphoma treatment protocols varied. These factors could independently affect survival time.

This study found that the group of cats most likely to have a shorter survival time were those with large cell lymphoma that—within the first month of chemotherapy—lost more than 5% of their body weight

Krick EL, Moore RH, Cohen RB, et al. Prognostic significance of weight changes during treatment of feline lymphoma. *J Fel Med Surg* 2011; 13:976-983.

CSBD = chronic small bowel disease; GI = gastrointestinal; HE = hemotoxylin and eosin; IBD = inflammatory bowel disease; IHC = immunohistochemistry; PARR = PCR for Antigen Receptor Rearrangement; PCR = polymerase chain reaction

Resources

Daniaux LA, Laurenson MP, Marks SL, et al. Ultrasonographic thickening of the muscularis propria in feline small intestinal small cell T-cell lymphoma and inflammatory bowel disease. *J Fel Med Surg* 2014; 16(2):89-98; abstract and access to full text available at **http://jfm.sagepub.com/content/16/2/89.abstract**.

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