Compendium

Feline Small Cell Lymphosarcoma Versus Inflammatory Bowel Disease: Diagnostic Challenges

Suliman Al-Ghazlat, DVM, DACVIM
Christian Eriksson de Rezende, DVM, MS
Jean Ferreri, DVM, DACVIM
BluePearl Veterinary Partners
New York, New York

Abstract: *Inflammatory bowel disease (IBD) and small cell lymphosarcoma (SCLSA) are common causes of chronic gastrointestinal (GI) tract disease in cats. The history, clinical signs, and results of blood work and imaging for these conditions are nonspecific and often overlap. After a thorough diagnostic workup and treatment trials to rule out other conditions, a definitive diagnosis requires histopathologic evaluation of GI tract biopsy specimens. Full-thickness tissue samples appear to be superior to endoscopic biopsy samples in providing an accurate diagnosis. Adding advanced diagnostics such as polymerase chain reaction and immunohistochemistry to traditional histopathology may improve the diagnostic utility of small samples such as the ones obtained via endoscopy. Treatment of and prognosis for IBD and SCLSA are discussed in a* ***companion article****.*

For more information, please see the companion article, "Feline Small Cell Lymphosarcoma Versus Inflammatory Bowel Disease: Treatment and Prognosis ."

Inflammatory bowel disease (IBD) refers to a group of idiopathic, chronic gastrointestinal (GI) tract disorders characterized by persistent or recurrent GI signs and inflammation of the GI tract.[1,2] The etiology of IBD is multifactorial and is, at least in part, mediated via inappropriate and uncontrolled inflammation of gut-associated lymphoid tissue against harmless environmental antigens such as those present in food and commensal bacteria.[1–4]

IBD was first reported in small animals around 25 years ago; today, it is the most common diagnosis in cats and dogs with chronic GI tract disease.[1,2] The lack of clinical, diagnostic, histopathologic, and therapeutic standards has resulted in great challenges in the diagnosis and treatment of companion animal GI tract disorders and raised concerns regarding diagnosing IBD. The World Small Animal Veterinary Association (WSAVA) International GI Standardization Group and the American College of Veterinary Internal Medicine (ACVIM) have published multiple statements to provide guidelines and standards for performance and interpretation of various diagnostic tests in dogs and cats with GI diseases, including treatment trials, patient response, and outcome.[2,5] These statements stress that IBD should not be diagnosed based on histopathology alone and that obtaining biopsy samples from the GI tract is only one part of a comprehensive workup[2] (**BOX 1** and **BOX 2**).

Box 1. Criteria for the Clinical Diagnosis of Inflammatory Bowel Disease in Dogs and Cats[a]

- Chronic persistent or recurrent GI tract signs (for ≥2 weeks)
- Inability to document other causes of GI signs or/and inflammation
- Inadequate response to dietary, antimicrobial, and anthelmintic therapies alone
- Histopathologic evidence of mucosal inflammation
- Clinical response to antiinflammatory or immunosuppressive agents

[a]These criteria do not differentiate inflammatory bowel disease from lymphosarcoma.

Lymphosarcoma (LSA) is the most common type of hematopoietic neoplasia in cats.[6] Risk factors for feline LSA include FeLV or FIV infection, chronic inflammation, and exposure to cigarette smoke.[6–9] However, most cats with GI tract LSA are negative for FeLV/FIV infection.[6] *Helicobacter* infection may also play a role in the pathogenesis of the disease.[10] LSA can occur in multiple anatomic locations, but the GI tract is the most common in cats.[6] Over time, there has been an apparent increase in localization of LSA to the GI tract in cats.[6–11]

Clinically and histologically, LSA is divided into lymphocytic, low-grade, small cell LSA (SCLSA) or lymphoblastic, high-grade, large cell LSA (LCLSA).[12,13] A separate, rare histologic type of GI

Box 2. Suggested Workup for Cats With GI Tract Disease Before Biopsy

- Perform a complete blood count, biochemistry profile, urinalysis, and thyroid evaluation to look for underlying or concurrent diseases.
- Perform fecal testing for GI parasites.
- Perform abdominal ultrasonography to evaluate the extraintestinal organs in addition to GI tract wall thickness, layering, and motility.
- Measure vitamin B_{12} level to assess disease severity and localization and the need for supplementation.
- Perform treatment trials for food intolerance and GI parasites when appropriate in stable patients.
- Measure fTLI to test for exocrine pancreatic insufficiency in cats with diarrhea and/or weight loss.
- Measure fPLI to test for pancreatitis in cats with vomiting and/or decreased appetite.
- Perform thoracic radiography to look for evidence of metastatic disease or concurrent cardiac or pulmonary diseases.

fPLI = serum feline pancreatic lipase immunoreactivity, *fTLI* = serum feline trypsin-like immunoreactivity.

tract LSA, large granular lymphocyte lymphosarcoma, has also been described.[14] This type carries a grave prognosis. LCLSA often has an acute clinical presentation and is fairly easily recognized histologically due to its distinct cellular morphology. SCLSA is a slowly progressive neoplasm that is characterized by infiltration of well-differentiated small lymphocytes.[12] Cats with SCLSA often have a long clinical history before diagnosis.[12,15,16] One study showed that GI tract SCLSA is three times more common than LCLSA in cats.[13]

IBD and LSA are often the remaining differentials for a feline patient with chronic GI tract signs after a thorough, noninvasive diagnostic workup including therapeutic trials (**BOX 2**). The clinical history and findings from the physical examination; hematology, biochemistry, and imaging results; and even histopathologic changes of IBD and GI tract SCLSA often overlap.[16]

Signalment

There is no clear sex, age, or breed predisposition for feline IBD or LSA.[13,17,18] However, in some studies, males appear to be predisposed to GI tract LSA.[13,17,18] Cats with LSA tend to be older, with a median age of 9 to 13 years; however, GI tract LSA has been reported in cats 1 to 20 years of age.[13,17,18]

Clinical Signs

The common clinical signs of LSA and IBD are nonspecific and include any combination of weight loss, variation in appetite, vomiting, diarrhea, and lethargy.[13,17,18]

Physical Examination

Cats with IBD or LSA can have a normal physical examination. Abnormalities in both conditions may include thin body condition with muscle wasting, evidence of dehydration, thickened intestinal loops, and mesenteric lymphadenopathy.[13,17] In cats with LCLSA, abdominal masses may be palpated.

Clinical Pathology

Laboratory findings are often nonspecific; mild nonregenerative anemia, neutrophilia, and mild hypoalbuminemia have been frequently reported in cats with LSA.[15,17,19] Hypoalbuminemia is rare in cats with IBD. Hypocobalaminemia is a frequent finding in both conditions and is an important therapeutic target.[20,21]

Imaging

Abdominal radiography is rarely useful in the diagnosis. Abdominal ultrasonography findings can be normal in some cases of IBD or LSA.[22] Common ultrasonographic findings in both conditions include generalized or regional gastric or intestinal wall thickening, mesenteric lymphadenopathy, and decreased motility.[22] Findings that suggest a neoplastic process and that should increase the indications for biopsy include loss of normal wall layering, disproportionally thick muscularis propria, focal intestinal mass effects, and ascites.[22,23]

Biopsy and Histopathology

A thorough diagnostic workup to rule out other causes is crucial. However, to confirm the diagnosis, histopathologic evaluation of appropriately collected GI tissue samples is required.

Problems in making the diagnosis may be encountered because of overlap in histologic features between IBD and LSA (predominantly SCLSA), differences of opinion among pathologists, inadequacy of tissue specimens, and the fact that if the pathologic process is segmental, sampling the wrong segment of the GI tract can result in misdiagnosis.[22,24–28] In addition, LSA and inflammatory infiltrates can coexist.[26,28] The potential for progression of IBD to LSA further complicates the diagnosis.[8,9] Mucosa-associated lymphoid tissues (MALT) are normally populated primarily by T lymphocytes, and in both IBD and SCLSA, the T-cell population expands beyond the MALT. However, in contrast to IBD, neoplastic cells frequently infiltrate beyond the mucosa, destroying normal tissue architecture.[28] Therefore, biopsy specimens of intestinal LSA in which neoplastic cells do not extend beyond the mucosa and endoscopic biopsy specimens, in which histologic evaluation is often limited to the mucosa, are especially difficult for pathologists to interpret.

For clinicians, the most challenging question associated with GI tract biopsy is how to obtain tissue samples of adequate depth and at the correct anatomic location. Whether to obtain full-thickness biopsy (FTB) or endoscopic biopsy (EB) samples has been a subject of discussion over the past decade. Benefits of EB include the ability (1) to see mucosal changes and lesions[2] (e.g., ulceration, erosion, lymphangiectasia), enabling directed biopsy of these sites; (2) to collect multiple tissue samples (e.g., 10 or more) from each site, as some diseases may have a multifocal distribution, even within the same section of the intestine; and (3) to begin antiinflammatory or chemotherapeutic agents without delay after the procedure. On the other hand, EB is limited to

the proximal GI tract (stomach and duodenum) and colon and distal ileum.

Surgery or laparoscopy permits the collection of transmural samples of any segment of the GI tract in addition to samples from other organs (lymph nodes, liver, and pancreas). In rare cases of intestinal perforation or obstruction, surgery can also have a therapeutic role.

Full-Thickness Versus Endoscopic Biopsy Samples

In 2006, Evans et al[16] concluded that EB samples are not adequate for differentiating IBD from LSA in the small intestine. In a prospective study of 22 cats with IBD or GI tract LSA, EB specimens of the stomach and duodenum were obtained immediately before laparotomy or laparoscopic surgery, during which FTB specimens were obtained from the stomach, duodenum, jejunum and the ileum. LSA was diagnosed in 10 cats based on analysis of the FTB specimens. LSA was detected in the jejunum and ileum in all 10 of these cats and in the duodenum in nine cats. However, based on analysis of the EB samples, of the nine cats with LSA in the duodenum, one had a diagnosis of LSA, three had findings suggestive of LSA, and five had a diagnosis of IBD. This is the most commonly cited study to show the superiority of FTB over EB. It highlights some of the serious limitations of endoscopy, as of the five cats with LSA diagnosed as IBD on duodenal EB, two underwent only partial duodenal assessment and in three, duodenal biopsy had been performed blindly. Overall, in eight out of 22 cats, the pylorus could not be passed with the endoscope. and three duodenal samples were obtained blindly. Despite this study's findings, the 2010 ACVIM Consensus Statement recommended that where biopsy of the GI tract is indicated, EB is the preferred choice.[2]

Kiupel et al published a retrospective study on jejunal and ileal tissue samples (50 FTB, 13 EB) collected from a total of 63 cats.[28] In 39 cases, the lymphocytic infiltration extended into the submucosa; 95% (37 of 39) of these cases were diagnosed as LSA. Lymphocyte infiltration was seen in 28 of 50 tunica muscularis samples; 27 of these cases were diagnosed as LSA. Of 49 samples that included serosa, 22 had serosal infiltration, and all 22 of these cases were diagnosed as LSA.

Because infiltration of lymphocytes deeper than the mucosa is a major criterion for LSA diagnosis, FTB specimens appear to be superior to EB specimens for differentiating LSA from IBD. On the other hand, in many cats diagnosed with LSA in the Kiupel et al study, the infiltrate was limited to the mucosa. For example, intramuscular infiltrates were present in only 20 of 34 cases of LSA that were diagnosed from FTB specimens.[28] In other words, although tunica muscularis infiltration has excellent specificity (96%) for LSA, it only occurred in 59% of cats with LSA. An earlier study by Kleinschmidt et al on 43 cats with inflammatory and noninflammatory diseases of the GI tract also showed a diagnostic advantage for FTB samples.[29] This study also showed an advantage for sampling all the segments of the GI tract, the liver, and the mesenteric lymph nodes. Three out of 10 cats diagnosed with LSA in the Kleinschmidt study would have been misdiagnosed as IBD if samples were collected from only the stomach, duodenum, and colon.

Duodenal Versus Ileal Endoscopic Biopsy Samples

Recently, an excellent retrospective study strongly questioned the accuracy of obtaining endoscopic samples from the duodenum alone.[30] In the study, a diagnosis of LSA was made in 18 of 70 cats based on duodenal and/or ileal EB samples. Eight cats were diagnosed with only ileal LSA, seven were diagnosed with only duodenal LSA, and three were diagnosed with LSA in the ileum and the duodenum. In other words, a standard gastroduodenoscopy in this population would have resulted in misdiagnosing 44% of cats. The study showed a clear diagnostic advantage to obtaining both duodenal and ileal tissues samples when endoscopy of the GI tract is performed.

Immunohistochemistry and Polymerase Chain Reaction

As discussed above, differentiation of GI tract SCLSA from IBD based on histopathology using only hematoxylin-eosin (HE) staining is problematic. Detection of a clonal population of cells (cells from a single origin) in a lymphoproliferative lesion is an important criterion for the diagnosis of neoplasia.[28,31] Polymerase chain reaction (PCR) can be used to detect clonality in lymphocytes. PARR (polymerase chain reaction for antigen receptor rearrangement) tests for specific mutations in the lymphoid genome that are found in many cases of lymphoid neoplasia. This test is used to help make a definitive diagnosis of lymphoid neoplasia if results of other tests are equivocal.

Immunohistochemistry (IHC) is used clinically to immunophenotype cells with fluorescent-labeled antibodies raised against specific cell surface proteins to assess the phenotypic uniformity of a mucosal infiltrate.[26–28] The pattern of positive and negative interactions with the various antibodies yields a diagnosis of cell lineage and, if applicable, lymphoid immunophenotype. Besides its value in reaching a diagnosis, immunophenotyping might be of prognostic value in cases of feline GI tract LSA.[32] Both IHC and PCR can be performed on formalin-fixed tissue.

In 2005, a study was published in which samples from 32 cats with a histopathologic diagnosis of GI

Key Points

- IBD cannot be diagnosed based on histopathology alone. A thorough diagnostic workup and treatment trials are needed to rule out other causes for GI tract signs.
- The overlap in histologic features, differences of opinion among pathologists, inadequacy of tissue specimens, regional nature of the pathologic process and the fact that LSA and IBD can coexist make the differentiation between the two conditions very challenging.
- Clinicians should attempt to collect duodenal and ileal tissue samples when EB is performed.
- IHC and PCR are promising adjunctive diagnostics and will likely improve the ability to differentiate IBD from LSA.

tract LSA or multicentric LSA affecting the GI tract were reevaluated using histopathology and IHC.[27] This reevaluation resulted in five cases being redefined as probable inflammatory enteropathy rather than LSA. This study suggested that IHC is a useful adjunct to histopathology and may help in distinguishing LSA from severe GI tract inflammation.

In another study published in 2005, PCR was used to determine molecular clonality in samples from cats with diagnosed intestinal IBD (nine cats), or transmural and mucosal T-cell LSA (28 cats).[31] Clonal rearrangement was detected in 22 of 28 cases of intestinal T-cell LSA, and oligoclonality was detected in three cases of intestinal T-cell LSA. In contrast, polyclonal rearrangement was detected in all normal intestinal tissues (three cats) and in all nine cats with IBD. If the clonal and oligoclonal results are combined, the sensitivity of clonality detection was 89%. Failure to detect clonal T-cell populations occurred in three cats (11%) with T-cell LSA. The study showed that the sensitivity of the PCR assay makes it useful for the detection of clonal rearrangements in small amounts of tissue, such as EB samples.

Combining Histopathology, Immunohistochemistry, and Polymerase Chain Reaction Testing

The main goal of Kiupel's study was to evaluate the impact of adding IHC and PCR results for lymphocyte clonality to the routine diagnosis of LSA or inflammation based on microscopic examination of HE stained sections alone.[28] All of the patients were diagnosed with either IBD (19 cases, 30%) or intestinal LSA (44 cases, 70%), based on routine histopathologic examination alone. Ten of the 19 cases (53%) that originally had been diagnosed as IBD by histopathologic examination alone were reclassified as LSA when IHC and PCR results were evaluated in conjunction with the HE findings. Three of the 47 cases (6%) that originally had been diagnosed as LSA by histopathologic examination alone were reclassified as IBD when IHC and PCR results were added. The study demonstrates that combining the histopathologic evaluation with IHC of the lymphocytic infiltration and analysis of clonality by PCR results in a more accurate differentiation of neoplastic from inflammatory lymphoid cells.

Summary

Differentiating low-grade SCLSA from IBD in cats is challenging. Based on the current literature, owners should be educated about the likely superiority of FTB over EB in obtaining an accurate diagnosis. In our experience, after this discussion, many owners still choose to proceed with EB for reasons related to perceived invasiveness, the critical nature of some patients, and cost. When endoscopy is performed, obtaining duodenal and ileal samples should be attempted. Systematic assessment of samples using routine histopathology, IHC, and PCR may help decrease the likelihood of misdiagnosis, especially with endoscopic samples.

References

1. Jergens AE, Moore FM, Haynes JS, et al. Idiopathic inflammatory bowel disease in dogs and cats: 84 cases (1987–1990). *J Am Vet Med Assoc* 1992;201(10):1603-1608.
2. The WSAVA International Gastrointestinal Standardization Group, Washabau RJ, Day MJ, Willard MD, et al. Endoscopic, biopsy, and histopathologic guidelines for the evaluation of gastrointestinal inflammation in companion animals. *J Vet Intern Med* 2010;24(1):10-26.
3. Waly NE, Stokes CR, Gruffydd-Jones TJ, et al. Immune cell populations in the duodenal mucosa of cats with inflammatory bowel disease. *J Vet Intern Med* 2004;18(6):816-825.
4. Xavier RJ, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. *Nature* 2007;448:427-434.
5. Day MJ, Bilzer T, Mansell J, et al. Histopathological standards for the diagnosis of gastrointestinal inflammation in endoscopic biopsy samples from the dog and cat. World Small Animal Veterinary Association Gastrointestinal Standardization Group. *J Comp Pathol* 2008;137:S1-S43.
6. Louwerens M, London CL, Pedersen NC, et al. Feline lymphoma in the post-feline leukemia virus era. *J Vet Intern Med* 2005;19(4):329-335.
7. Bertone ER, Snyder LA, Moore AS. Environmental tobacco smoke and risk of malignant lymphoma in pet cats. *Am J Epidemiol* 2002;156(3):268-273.
8. Hart JR, Shaker E, Patnaik E, Garvey MS. Lymphocytic-plasmacytic enterocolitis in cats: 60 cases (1988–1990). *J Am Anim Hosp Assoc* 1994;30:505-514.
9. Davenport DJ, Leib NS, Roth L. Progression of lymphocytic-plasmacytic enteritis to gastrointestinal lymphosarcoma in three cats. *Proc Vet Cancer Soc 7th Annu Conf* 1987 suppl:54-56.
10. Bridgeford EC, Marini RP, Feng Y, et al. Gastric *Helicobacter* species as a cause of feline gastric lymphoma. *Vet Immunol Immunopathol* 2008;123:106-113.
11. Mauldin GE, Mooney SC, Meleo KA, et al. Chemotherapy in 132 cats with lymphoma (1988–1994). *Proc Vet Cancer Soc 15th Annu Conf* 1995:35-36.
12. Lingard AE, Briscoe K, Beatty JA, et al. Low-grade alimentary lymphoma (LGAL): clinicopathological findings and response to treatment in 17 cases. *J Feline Med Surg* 2009;11:692-700.
13. Fondacaro JV, Richter KP, Carpenter JL, et al. Feline gastrointestinal lymphoma: 67 cases. *Eur J Comp Gastroenterol* 1999;4(2):69-74.
14. Krick EL, Little L, et al. Description of clinical and pathological findings, treatment and outcome of feline large granular lymphocyte lymphoma (1996-2004). *Vet Comp Oncol* 2008;6(2):102-110.
15. Carreras JK, Goldschmidt M, Lamb M, et al. Feline epitheliotropic intestinal malignant lymphoma: 10 cases (1997–2000). *J Vet Intern Med* 2003;17(3):326-331.
16. Evans SE, Bonczynski JJ, Broussard JD, et al. Comparison of endoscopic and full-thickness biopsy specimens for diagnosis of inflammatory bowel disease and alimentary tract lymphoma in cats. *J Am Vet Med Assoc* 2006;229(9):1447-1450.
17. Mahony OM, Moore AS, Cotter SM, et al. Alimentary lymphoma in cats: 28 cases (1988–1993). *J Am Vet Med Assoc* 1995;207(12):1593-1597.
18. Zwahlen CH, Lucroy MD, Kraegel SA, et al. Results of chemotherapy for cats with alimentary malignant lymphoma: 21 cases (1993–1997). *J Am Vet Med Assoc* 1998;213(8):1144-1149.
19. Gabor LJ, Canfield PJ and Malik R. Haematological and biochemical findings in cats in Australia with lymphosarcoma. *Aust Vet J* 2000;78:456-461.
20. Ruaux CG, Steiner JM, Williams DA. Early biochemical and clinical responses to cobalamin supplementation in cats with signs of gastrointestinal disease and severe hypocobalaminemia. *J Vet Intern Med* 2005;19(2):155-160.
21. Kiselow MA, Rassnick KM, McDonough SP, et al. Outcome of cats with low-grade lymphocytic lymphoma: 41 cases (1995–2005). *J Am Vet Med Assoc* 2008;232(3):405-410.
22. Gaschen L. Ultrasonography of small intestinal inflammatory and neoplastic diseases in dogs and cats. *Vet Clin North Am Small Anim Pract* 2011;41:329-344.
23. Zwingenberger AL, Marks SL, Baker TW, et al. Ultrasonographic evaluation of the muscularis propria in cats with diffuse small intestinal lymphoma or inflammatory bowel disease. *J Vet Intern Med* 2010;24(2):289-292.
24. Willard MD, Jergens AE, Duncan RB, et al. Interobserver variation among histopathologic evaluations of intestinal tissues from dogs and cats. *J Am Vet Med Assoc* 2002;220(8):1177-1182.
25. Willard MD, Mansell J, Fosgate GT, et al. Effect of sample quality on the sensitivity of endoscopic biopsy for detecting gastric and duodenal lesions in dogs and cats. *J Vet Intern Med* 2008;22(4):1084-1089.
26. Briscoe KA, Krockenberger M, Beatty JA, et al. Histopathological and immunohistochemical evaluation of 53 cases of feline lymphoplasmacytic enteritis and low-grade alimentary lymphoma. *J Comp Pathol* 2011;145:187-198.
27. Waly NE, Gruffydd-Jones TJ, Stokes CR, et al. Immunohistochemical diagnosis of

alimentary lymphomas and severe intestinal inflammation in cats. *J Comp Pathol* 2005; 133:253-260.
28. Kiupel M, Smedley RC, Pfent C, et al. Diagnostic algorithm to differentiate lymphoma from inflammation in feline intestinal biopsy specimens. *Vet Pathol* 2011;48:212-222.
29. Kleinschmidt S, Harder J, Nolte I, et al. Chronic inflammatory and non-inflammatory diseases of the gastrointestinal tract in cats: diagnostic advantages of full-thickness intestinal and extraintestinal biopsies. *J Feline Med Surg* 2010;12:97-103.
30. Scott KD, Zoran DL, Mansell J, et al. Utility of endoscopic biopsies of the duodenum and ileum for the diagnosis of inflammatory bowel disease and small cell lymphoma in cats. *J Vet Intern Med* 2011;25(6):1253-1257.
31. Moore PF, Woo JC, Vernau W, et al. Characterization of feline T-cell receptor gamma (TCRG) variable region genes for the molecular diagnosis of feline intestinal T-cell lymphoma. *Vet Immunol Immunopathol* 2005;106:167-178.
32. Patterson-Kane JC, Kugler BP, Francis K. The possible prognostic significance of immunophenotype in feline alimentary lymphoma: a pilot study. *J Comp Pathol* 2004; 130:220-222.

CE
3 CE Credits

*This article qualifies for 3 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. CE tests must be taken online at **Vetlearn.com**; test results and CE certificates are available immediately. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program.*

1. **Which of the following is not a criterion for the diagnosis of IBD?**
   - **a.** histopathologic evidence of mucosal inflammation
   - **b.** inability to document other causes of gastrointestinal signs and/or inflammation
   - **c.** chronic persistent or recurrent GI tract signs (for ≥2 weeks)
   - **d.** a complete clinical response to a well-designed dietary trial

2. **Which statement is correct regarding LSA in cats?**
   - **a.** Small-cell LSA (SCLSA) is an acute disease with short clinical history and rapid deterioration.
   - **b.** Most cats with GI tract LSA are positive for FeLV.
   - **c.** The most common anatomic location for feline LSA is the GI tract.
   - **d.** It is often difficult to differentiate SCLSA from large-cell LSA based on histopathology.

3. **Which of the following statements is correct regarding the diagnostic workup for a cat suspected of having SCLSA or IBD?**
   - **a.** It is usually easy to differentiate between the two conditions based on the history and the physical examination.
   - **b.** Abdominal ultrasonography can usually differentiate SCLSA from IBD.
   - **c.** A normal abdominal ultrasound can rule out SCLSA.
   - **d.** Increased thickness of the muscularis layer on ultrasonography is suggestive of SCLSA.

4. **Which of the following statements is false with regard to surgical exploration?**
   - **a.** It allows full-thickness biopsy of the GI tract.
   - **b.** It is the method of choice to diagnose gastric ulcers.
   - **c.** It allows biopsy of organs outside the GI tract.
   - **d.** Samples obtained during this procedure may be superior to EB for differentiating IBD from SCLSA.

5. **When endoscopy is performed in a cat to confirm the diagnosis of IBD versus SCLSA, the clinician should attempt to collect samples from which locations?**
   - **a.** stomach only
   - **b.** stomach and jejunum
   - **c.** jejunum and duodenum
   - **d.** duodenum and ileum

6. **Which statement is false with regard to standard GI tract endoscopy in veterinary medicine?**
   - **a.** It allows the collection of multiple mucosal samples of all GI tract segments.
   - **b.** It is less invasive than laparoscopy and surgery.
   - **c.** It allows the clinician to directly diagnose lesions such as ulcers and lymphangiectasia.
   - **d.** It allows initiation of antiinflammatory or chemotherapeutic therapy directly after the procedure.

7. **Histopathologic differentiation between IBD and SCLSA is challenging because**
   - **a.** the histologic features of IBD and SCLSA overlap.
   - **b.** pathologists' interpretations can differ.
   - **c.** SCLSA and inflammatory infiltrates can coexist.
   - **d.** all of the above

8. **Which statement is false with regard to polymerase chain reaction (PCR) testing?**
   - **a.** It can be used to detect clonality in lymphocytes.
   - **b.** The sensitivity of PCR makes it useful for the detection of clonal rearrangements in small amounts of tissue.
   - **c.** If PCR fails to detect clonality, LSA can be ruled out.
   - **d.** It is a promising test to help differentiate IBD from LSA.

9. **Immunohistochemistry (IHC) may be useful for**
   - **a.** determining the phenotypic uniformity of lymphocytes.
   - **b.** differentiating lymphocytic inflammation from neoplasia.
   - **c.** obtaining more information regarding the prognosis of LSA.
   - **d.** all of the above

10. **Which statement regarding diagnosis of IBD versus LSA is most accurate?**
    - **a.** Histopathology of hematoxylin-eosin–stained samples always differentiates IBD from LSA.
    - **b.** Studies have proved that full-thickness and endoscopic biopsy samples are equivalent for diagnostic testing using histopathology.
    - **c.** PCR and IHC results may change initial diagnoses based on histopathology alone.
    - **d.** Biopsy results alone are adequate for diagnosing IBD or LSA.