Comparison of gastric and duodenal lesions in dogs and cats with and without lymphocytic-plasmacytic enteritis

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Objective—To compare histologic lesions in the stomach and duodenum of dogs and cats with and without lymphocytic-plasmacytic enteritis (LPE).

Design—Case-control study.

Animals—20 clinically normal dogs, 40 dogs with LPE, 10 clinically normal cats, and 20 cats with LPE.

Results—Unevenness of the mucosal surface was detected in the stomach of 4 of the 20 (20%) clinically normal dogs and 10 of the 40 (25%) dogs with LPE. Mucosal friability was detected in the duodenum of 16 (40%) of the dogs with LPE and 10 of the 20 (50%) cats with LPE. Histologically, clinically normal dogs and dogs with LPE had various degrees of fibrosis in the gastric lamina propria. All of the clinically normal cats and the cats with LPE had slight gastric fibrosis. Clinically normal cats had infiltrates of inflammatory cells similar to those seen in the clinically normal dogs. Significantly more plasma cells and lymphocytes were seen in the duodenal lamina propria of dogs and cats with LPE than in the duodenal lamina propria of clinically normal animals.

Clinical Implications—LPE should be diagnosed by counting the number of inflammatory cells in the duodenal lamina propria and then comparing that number with the number seen in clinically normal animals. (*J Am Vet Med Assoc* 1996;209:95–97)

Lymphocytic-plasmacytic enteritis (LPE), an inflammatory intestinal disease characterized by excessive infiltration of the intestinal mucosa by lymphocytes and plasma cells, has been reported in dogs and cats since the 1980s and is considered by most investigators to be the most common inflammatory bowel disease in dogs and cats.[1-6] Endoscopic examination of the mucosa of the stomach and duodenum and histologic examination of mucosal biopsy specimens obtained during endoscopy have been used to aid in the evaluation of dogs and cats suspected to have LPE.[7-10] The purpose of the study reported here was to compare histologic lesions in the stomach and duodenum of dogs and cats with and without LPE.

Materials and Methods

Animals—Twenty clinically normal dogs (7 males and 13 females) between 8 months and 10 years old (mean, 4.5 years); 40 dogs in which LPE has been diagnosed (18 males and 22 females) between 5 months and 13 years old (mean, 5.8 years); 10 clinically normal cats (5 males and 5 females) between 6 months and 8 years old (mean, 2.7 years); and 20 cats in which LPE has been diagnosed (8 males and 12 females) between 7 months and 10 years old (mean, 4.6 years) were included in the study. The animals belonged to individuals living in Oita or Fukuoka prefectures, Japan, and were of various breeds. They were donated to us during the study and were returned to their owners at the end of the study. Dogs and cats included in the study were considered to be clinically normal if they had not had any episodes of vomiting, diarrhea, weight loss, or listlessness in the previous 3 months. Dogs and cats were considered to have LPE if they had had clinical signs of persistent gastroenteritis (ie, vomiting, diarrhea, weight loss) for > 10 days, and if results of CBC and serum biochemical analyses were within reference ranges, results of fecal float examinations for parasites and parasite ova were negative, results of abdominal radiography and ultrasonography did not indicate any other abnormality, and clinical signs resolved after treatment with prednisone (2.0 mg/kg of body weight, IM). Physical, hematologic, and serum biochemical examinations were performed in all dogs and cats, and fecal examinations also were done 2 or 3 times in each animal before the endoscopic examination.

Endoscopic technique—Food was withheld for 12 to 24 hours. Anesthesia was induced by IM administration of ketamine hydrochloride and acepromazine maleate and maintained with halothane. Endoscopy was performed using a flexible, fiberoptic endoscope with an external diameter of 7.9 mm and a 2.0-mm-diameter biopsy channel.[a] The animal was positioned in left lateral recumbency, and the stomach and duodenum were examined by 2 of the authors (HS, TT). Mucosal samples were obtained from the fundus and pylorus of the stomach and from the duodenum, using endoscopic forceps.[b] Two samples were obtained from each area.

Morphologic studies—Gastric and duodenal samples were fixed in 10% formalin solution for 2 days. Tissues were dehydrated, embedded in paraffin wax, cut into 3-µm thick sections, and stained with H&E. Selected sections also were stained with azan, Weigert's fibrin, and van Gieson's elastica stains. Sections were examined by one of the authors (KY), using light microscopy, and the examiner was not aware of which animals had LPE. The extent of fibrosis in the gastric or duodenal lamina propria was graded as follows: grade 0, no fibrosis; grade 1, between 1 and 30% of the lamina propria was affected; grade 2, between 31 and 60% of the lamina propria was affected; grade 3, between 61 and 100% of the lamina propria was affected. Inflammatory cells were counted in 12 areas of 5,000 µm² selected at random from the lamina propria of each of the 2 samples from the fundus and pylorus. The mean number of cells/5,000 µm² was calculated. For each animal, cellular infiltration of the gastric lamina propria was graded on the basis of mean cell number as follows: grade 0, < 20 inflammatory cells/5,000 µm²; grade 1, 20 to 25 cells/5,000 µm²; grade 2, 26 to 30 cells/5,000 µm²; grade 3, > 30 cells/5,000 µm². Inflammatory cells in the duodenal lamina propria were counted by examining, on each section, 2 areas of 5,000 µm² near the apex of the villi, 2 areas of 5,000 µm² near the base of the villi, and 2 areas of 5,000 µm² in the deeper portion of the lamina propria. Mean cell number for the 12 areas was calculated. For each animal,

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Table 1—Grade of fibrosis in the gastric lamina propria of clinically normal dogs and cats, and dogs and cats with lymphocytic plasmacytic enteritis (LPE)

Group	No. affected			
	Grade 0*	Grade 1	Grade 2	Grade 3
Clinically normal dogs (n = 20)	5	7	4	4
Dogs with LPE (n = 40)	6	16	14	4
Clinically normal cats (n = 10)	0	10	0	0
Cats with LPE (n = 20)	0	20	0	0

*Grade 0, no fibrosis; grade 1, slight fibrosis; grade 2, moderate fibrosis; grade 3, severe fibrosis.

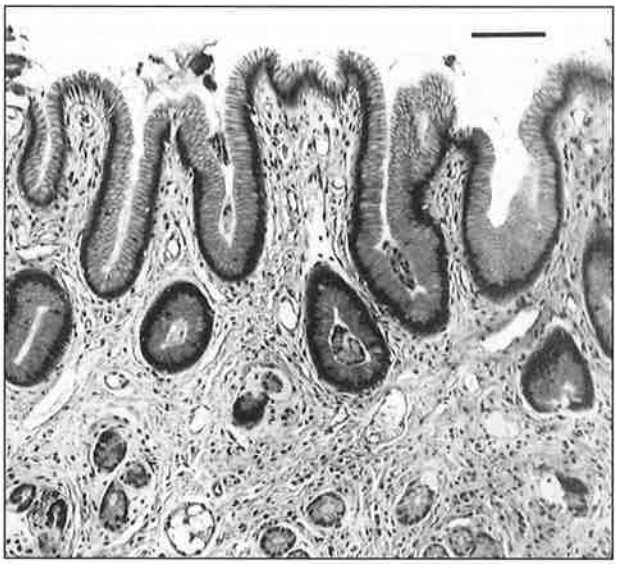

Figure 1—Photomicrograph of a section of stomach from a clinically normal 9-year-old dog. Notice the fibrosis in the lamina propria. Only a few glands are seen. H&E stain; bar = 100 μm.

Table 2—Grade of cell infiltration in the gastric lamina propria of clinically normal dogs and cats, and dogs and cats with LPE

Group	No. affected			
	Grade 0*	Grade 1	Grade 2	Grade 3
Clinically normal dogs (n = 20)	20	0	0	0
Dogs with LPE (n = 40)	35	2	2	1
Clinically normal cats (n = 10)	10	0	0	0
Cats with LPE (n = 20)	20	0	0	0

*Grade 0, < 20 inflammatory cells/5,000 μm^2; grade 1, 20 to 25 cells/5,000 μm^2; grade 2, 26 to 30 cells/5,000 μm^2; grade 3, > 30 cells/5,000 μm^2.

Table 3—Grade of cell infiltration in the duodenal lamina propria of clinically normal dogs and cats, and dogs and cats with LPE

Group	No. affected				
	Grade 0*	Grade 1	Grade 2	Grade 3	Grade 4
Clinically normal dogs (n = 20)	16	4	0	0	0
Dogs with LPE (n = 40)	0	3	13	12	12
Clinically normal cats (n = 10)	10	0	0	0	0
Cats with LPE (n = 20)	0	3	3	6	8

*Grade 0, < 40 inflammatory cells/5,000 μm^2; grade 1, 40 to 45 cells/5,000 μm^2; grade 2, 46 to 50 cells/5,000 μm^2; grade 3, 51 to 55 cells/5,000 μm^2; grade 4, > 55 cells/5,000 μm^2.

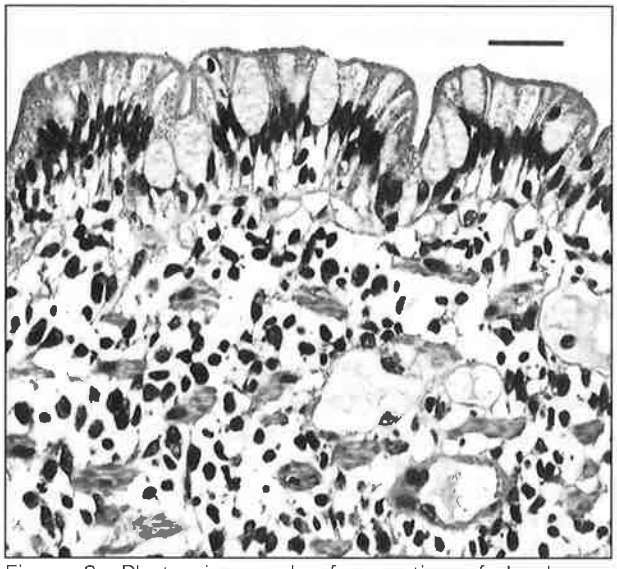

Figure 2—Photomicrograph of a section of duodenum from a clinically normal 9-year-old dog. Inflammatory cells can be seen in the lamina propria of the villus. H&E stain; bar = 25 μm.

cellular infiltration of the duodenal lamina propria was graded on the basis of mean cell number as follows: grade 0, < 40 inflammatory cells/5,000 μm^2; grade 1, 40 to 45 cells/5,000 μm^2; grade 2, 46 to 50 cells/5,000 μm^2; grade 3, 51 to 55 cells/5,000 μm^2; grade 4, > 55 cells/5,000 μm^2.

Statistical analysis—The significance of differences between the mean numbers of inflammatory cells in the duodenal lamina propria of clinically normal animals and animals with LPE was tested by use of the Mann-Whitney test.

Results

Gross findings—Unevenness of the mucosal surface was detected in the stomach of 4 of the 20 (20%) clinically normal dogs and 10 of the 40 (25%) dogs with LPE. Abnormalities were not detected in the stomach of any of the cats. Mucosal friability, defined as mucosal destruction and hemorrhage when the mucosa was gently touched with the endoscope, and mucosal irregularities were detected in the duodenum of 16 of the 40 (40%) dogs with LPE and 10 of the 20 (50%) cats with LPE, but not in the duodenum of any of the clinically normal dogs and cats.

Morphologic findings—Biopsy specimens of the stomach and duodenum included the mucosa and a portion of the submucosa. Clinically normal dogs and dogs with LPE had various degrees of fibrosis in the gastric lamina propria (Table 1), but we did not detect a difference in prevalence of gastric fibrosis between groups. In dogs with grade-3 fibrosis, only a few fundic and pyloric glands were seen (Fig 1). All of the clinically normal cats and the cats with LPE had grade-1 gastric fibrosis. Some dogs with LPE had increased numbers of inflammatory cells in the gastric lamina propria (Table 2).

Inflammatory cells, including lymphocytes, histiocytes, plasma cells, and eosinophils, were seen in the duodenal lamina propria from clinically normal dogs (Table 3, Fig 2). These cells were scanty in the apical

Table 4—Mean ± SD number of inflammatory cells in the duodenal lamina propria of clinically normal dogs and cats, and dogs and cats with LPE; twelve 5,000-μm² areas were examined in each animal

Group	Plasma cells/ 5,000 μm²	Lymphocytes/ 5,000 μm²	Histiocytes/ 5,000 μm²	Eosinophils/ 5,000 μm²	Total cells/ 5,000 μm²
Clinically normal dogs (n = 20)	2.9 ± 3.7*	27.4 ± 5.8	4.1 ± 3.2	0.3 ± 0.3	34.4 ± 9.7
Dogs with LPE (n = 40)	5.2 ± 2.8†	39.4 ± 5.4†	5.6 ± 2.7	0.3 ± 0.5	50.4 ± 4.2‡
Clinically normal cats (n = 10)	0.4 ± 0.4	17.5 ± 4.5	5.9 ± 1.5	0.1 ± 0.1	24.1 ± 5.4
Cats with LPE (n = 20)	2.7 ± 2.8†	40.5 ± 9.0†	7.3 ± 4.6	0.6 ± 0.6	51.3 ± 11.5†

*Mean ± SD cells/5,000 μm². †$P < 0.05$, compared with value for clinically normal animals. ‡$P < 0.01$, compared with value for clinically normal animals.

portion of the villi, and were seen primarily at the base of the villi and in the deeper portion of the lamina propria. Clinically normal cats had infiltrates of inflammatory cells similar to those seen in the dogs. Significantly more plasma cells and lymphocytes were seen in the duodenal lamina propria of dogs and cats with LPE than in the duodenal lamina propria of clinically normal animals (Table 4). Some dogs with LPE also had other mucosal changes, such as intraepithelial infiltration of lymphocytes, lamina proprial fibrosis, and villous lymphangiectasia. Similar changes were seen in cats with LPE.

Discussion

In this study, the prevalence of gastric lamina proprial fibrosis among clinically normal dogs and cats was high, compared with that in a previous report,[11] and we did not detect any difference between gastric fibrosis grades for clinically normal animals and animals with LPE. However, 4 of the 12 dogs with LPE that had grade-4 cellular infiltration in the duodenal lamina propria had grade-1 or higher cellular infiltration in the gastric lamina propria. This suggests that the role that the stomach plays in LPE should be further investigated.

There is little information on the number of inflammatory cells in the lamina propria of healthy animals of different breeds and ages.[12] In this study, inflammatory cells such as lymphocytes, plasma cells, histiocytes, and eosinophils were seen in the duodenal lamina propria of clinically normal dogs.

Our findings were essentially the same as those previously described for dogs and cats with LPE.[5,12,13] The number of inflammatory cells in animals with LPE was increased, compared with the number in clinically normal animals. A previously described method for diagnosing LPE relied on grading of lesions on the basis of numbers of leukocytes between colonic proprial glands.[10] However, this method reportedly is not well defined, so other investigators may find it difficult to apply this proposed scheme.[12] The measurement method used in the present study was considered to be objective and easy to apply in practice, because the inflammatory cells in the various areas of the lamina propria could be counted immediately. In our opinion, LPE should be diagnosed by counting the number of inflammatory cells in the duodenal lamina propria and then comparing that number with the number seen in clinically normal animals. We believe that an increase in the number of inflammatory cells in the lamina propria is the primary change in animals with LPE, and that alterations in mucosal structure are secondary to this increase.

In this study, a few of the clinically normal dogs had slightly high numbers of inflammatory cells in the duodenal lamina propria. It was difficult to determine whether these dogs were truly normal, but inflammatory cells can be seen in the intestinal lamina propria from clinically normal animals.[10]

[a]Olympus OES-10, Olympus Corp, Tokyo, Japan.
[b]FB-21K, Olympus Corp, Tokyo, Japan.

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