Clinical, clinicopathologic, radiographic, and ultrasonographic characteristics of intestinal lymphangiectasia in dogs: 17 cases (1996–1998)

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Objective—To characterize the clinical, clinicopathologic, and imaging findings in dogs with intestinal lymphangiectasia and to compare the histologic grade of lymphangiectasia with clinicopathologic and imaging abnormalities.

Design—Retrospective study.

Animals—17 dogs with a histologic diagnosis of intestinal lymphangiectasia.

Procedure—Medical records of dogs with a histologic diagnosis of intestinal lymphangiectasia were reviewed for signalment, history, clinical signs, results of exploratory laparotomy, and clinicopathologic, radiographic, ultrasonographic, and histologic findings.

Results—Mean age of dogs was 8.3 years; the most common clinical signs were diarrhea, anorexia, lethargy, vomiting, and weight loss. Abnormal physical examination findings included dehydration, ascites, and signs of pain on palpation of the abdomen. The most notable clinicopathologic findings were low serum ionized calcium concentration and hypoalbuminemia. Abdominal ultrasonography was performed in 12 dogs and revealed intestinal abnormalities in 8 dogs and peritoneal effusion in 7 dogs. Exploratory laparotomy revealed abnormalities in 9 of 16 dogs including thickened small intestine, dilated lacteals, lymphadenopathy, and adhesions. On histologic examination of the small intestine, concurrent inflammation was observed in 15 of 17 dogs, crypt ectasia in 5 of 17, and lipogranulomas in 2 of 17.

Conclusions and Clinical Relevance—Intestinal lymphangiectasia in dogs appears to be a heterogeneous disorder characterized by various degrees of panhypoproteinemia, hypocholesterolemia, lymphocytopenia, and imaging abnormalities. In most dogs, the severity of hypoalbuminemia appears to offer the best correlation with severity of histologic lesions of lymphangiectasia. Imaging abnormalities are common in dogs with intestinal lymphangiectasia but are not specific enough to differentiate this disorder from other gastrointestinal disorders, nor are they predictive of histologic severity. (J Am Vet Med Assoc 2001;219:197–202)
recorded at the time of initial examination. Abnormal physical examination findings were also recorded. The following findings were considered to be present only if recorded by the admitting clinician: signs of abdominal pain, thickened or fluid-filled intestine, ascites, hepatomegaly, and lymphadenopathy.

Records were reviewed for results of CBC, serum biochemical analyses, ionized calcium concentration, venous pH, coagulation profile, blood ammonia concentration, urinalysis, and urine protein:creatinine ratio determined prior to medical treatment. Serum total calcium concentration was adjusted for albumin concentration by use of the following equation: Corrected calcium concentration (mg/dl) = (calcium concentration [mg/dl] – albumin concentration [g/dl]) + 3.5. Urine was considered hyposthenuric, isosthenuric, or hypersthenuric if specific gravity was < 1.007, between 1.007 and 1.015, or > 1.015, respectively. Results of dipstick analysis of urine for protein, ketones, glucose, bilirubin, urobilinogen, and hemoglobin were recorded, and analytes were classified as absent or present (trace to +4). Partial thromboplastin time and prothrombin time were considered prolonged if values were > 125% than those of control samples. A concentration of fibrin split products > 10 µg/ml was considered abnormally high.

Thoracic and abdominal radiographs and abdominal sonograms were reviewed by a board-certified radiologist (HMS) who was blinded to the clinical signs and severity of histologic findings in the dogs. All radiographic abnormalities were documented. Abdominal ultrasonographic static images and reports were reviewed. In all dogs, a complete abdominal examination was performed, and all abnormalities were documented. Particular attention was paid to the appearance of the intestines and presence or absence of peritoneal effusion.

All dogs had an exploratory laparotomy in which a ventral midline incision was made, and a routine examination of the gastrointestinal tract was performed. In addition, there was direct examination of the pancreas, kidneys, mesenteric lymph nodes, liver, and biliary tract. After obtaining biopsy specimens, the abdomen was closed in a routine manner, and dogs were allowed to recover from anesthesia. Descriptive reports of the surgical procedure and abnormal findings at surgery were compiled and recorded by several surgeons.

Biopsy specimens of the small intestine were fixed in neutral-buffered 10% formalin and routinely processed for histologic examination. Five-micron-thick sections were cut from paraffin-embedded blocks and stained with H&E.

All specimens were reviewed by a board-certified pathologist (LEC). Lymphangiectasia was characterized as mild, moderate, or severe. The severity of lymphangiectasia was graded by counting the number of dilated lacteals per low power (10X objective) field. Three to 6 fields (depending on the size of the sample) were counted, and means were recorded. Sections with 8 or more dilated lacteals per low power field were graded as severe lymphangiectasia. Those with 4 to 7 dilated lacteals per low power field were graded as moderate lymphangiectasia. Those with 1 to 3 dilated lacteals per low power field were graded as mild.

Severity of inflammation in these small intestinal biopsy specimens was graded as previously described.8 Mild inflammation was characterized by low numbers of inflammatory cells without other changes. Moderate inflammation was characterized by high numbers of inflammatory cells with mild villous blunting and crypt separation. Severe inflammation was characterized by high numbers of inflammatory cells with considerable villous blunting and fusion, crypt separation and distortion, and fibrosis of the lamina propria. Concurrent inflammatory infiltrates were recorded as lymphocytic, plasmacytic, mixed lymphocytic-plasmacytic, eosinophilic, granulomatous, or mixed lymphocytic-plasmacytic and eosinophilic. The presence of crypt ectasia and intramural lipogranulomas was also recorded. Liver biopsy specimens that were collected at surgery were also examined for the presence of lymphangiectasia and lipogranulomas.

**Results**

Intestinal lymphangiectasia was confirmed histologically in 17 dogs. Eleven were spayed females, 5 were castrated males, and 1 was a sexually intact male. Mean age of affected dogs was 8.3 years (range, 2 to 14 years).

The most commonly affected breeds were Labrador Retrievers (3/17) and Yorkshire Terriers (3/17). The following breeds were also affected: mixed-breed (2), Dachshund (2), and 1 each of German Shepherd Dog, Rottweiler, Italian Greyhound, Bedlington Terrier, Miniature Poodle, Scottish Terrier, and Boxer.

The most common clinical signs were diarrhea (17/17), anorexia (14/17), lethargy (13/17), vomiting (11/17), and weight loss (8/17). Diarrhea was characterized as small intestinal in 9 dogs and large intestinal in 8; 1 dog had a history of melena. The onset of clinical signs was acute (<21 days) in 10 dogs and chronic (>21 days) in 7 dogs. Four dogs had a history of gastrointestinal tract disease, which included chronic small and large intestinal diarrhea (2/4), chronic small intestinal diarrhea (1/4), and parvoviral enteritis (1/4). One of these dogs with chronic small and large intestinal diarrhea had small intestinal biopsy specimens obtained previously via endoscopy; specimens contained dilated lymphatics in the mucosa, which are suggestive of IL.

Abnormal physical examination findings included dehydration (13/17), ascites (7/17), and signs of pain on abdominal palpation (6/17). Eight dogs were in normal body condition, 4 were underweight, 2 were overweight, 1 was cachectic, and 1 was obese. Data on body condition was not available for 1 dog.

Complete blood counts and biochemical analyses were performed in 14 and 13 dogs, respectively. Lymphocytopenia was detected in 8 of 14 dogs, hypoglobulinemia in 6, and hypocholesterolemia in 5. The most common abnormalities were hypoalbuminemia (10/13 dogs; median 2.12 ± 0.70 g/dl) and mild increases in alanine aminotransferase (ALT), alkaline phosphatase (ALP), and aspartate aminotransferase (AST) activities.

Serum ionized calcium concentration was mea-
teinuria and 2 dogs had 2+ proteinuria. In the 2 dogs, serum lipase activities (1,006 ± 803 and 1,108 ± 902 U/L, respectively) were within reference range. The other 2 dogs had no further assessment of liver function.

Serum amylase and lipase activities were determined in 6 and 7 dogs, respectively. Mean amylase and lipase activities (1,006 ± 803 and 1,108 ± 902 U/L, respectively) were within reference range.

Fecal flotations and bacteriologic cultures of feces were performed in 8 and 7 dogs, respectively. All results were negative for Salmonella spp., Campylobacter spp, and gastrointestinal parasites.

Coagulation profiles were performed in 10 dogs. Abnormal findings included pneumonia (3 dogs), evidence of hypovolemia (2), pleural effusion (2), and extraluminal lymphadenopathy (1). Both pneumonia and hypovolemia were found in 1 of these dogs. No abnormalities were evident in 6 dogs.

Abdominal radiography was performed in 6 dogs. Abnormal findings included pneumonia (3 dogs), evidence of hypovolemia (2), pleural effusion (2), and extraluminal lymphadenopathy (1). Both pneumonia and hypovolemia were found in 1 of these dogs. No abnormalities were evident in 6 dogs.

Abdominal ultrasonography was performed in 12 dogs; no abnormalities were evident in 2 dogs. Abnormal findings observed on the static images or documented in the ultrasound report included peritoneal effusion (7 dogs), thickening of the small intestinal wall (6), hyperechoic mesentery (5), hyperechoic small intestinal mucosal layer (5), small intestinal wall corrugation (2), large mesenteric lymph nodes (2), thickening of the gastric wall (1), indistinct small intestinal wall layering (1), hypermotility of the small intestine (1), dilated small intestinal lumen (1), and pancreatitis (1).

Abdominal ultrasonography was performed in 12 dogs and was below reference range values in all dogs tested (mean, 0.99 ± 0.19 mmol/L; reference range, 1.13 to 1.33 mmol/L). Venous pH was also measured in these 12 dogs and only 2 were mildly alkalotic. Serum corrected total calcium was decreased in 6/13 dogs (mean, 9.76 ± 1.11 mg/dL).

Urinalyses were performed in 9 dogs and proteinuria was detected in 6. Four dogs had trace or 1+ proteinuria and 2 dogs had 2+ proteinuria. In the 2 dogs with 2+ proteinuria, the specific gravity of the urine was > 1.050. Both dogs had concurrent hypoglobulinemia and hypoalbuminemia, and 1 had a urine protein:creatinine ratio of 0.32.

Of the 4 dogs with low serum albumin concentrations and serum globulin concentrations within reference range, 2 had blood ammonia concentrations within reference range. The other 2 dogs had no further assessment of liver function.

Thoracic radiography was performed in 13 dogs. Abnormal findings included pneumonia (3 dogs), evidence of hypovolemia (2), pleural effusion (2), and extraluminal lymphadenopathy (1). Both pneumonia and hypovolemia were found in 1 of these dogs. No abnormalities were evident in 6 dogs.

Abdominal ultrasonography was performed in 12 dogs; no abnormalities were evident in 2 dogs. Abnormal findings observed on the static images or documented in the ultrasound report included peritoneal effusion (7 dogs), thickening of the small intestinal wall (6), hyperechoic mesentery (5), hyperechoic small intestinal mucosal layer (5), small intestinal wall corrugation (2), large mesenteric lymph nodes (1), thickening of the gastric wall (1), indistinct small intestinal wall layering (1), hypermotility of the small intestine (1), dilated small intestinal lumen (1), and pancreatitis (1).

Exploratory laparotomy was performed on all dogs. Gross abnormalities recorded in the surgical reports included thickened small intestine (4 dogs), dilated lacteals (4), lymphadenopathy (2), and adhesions (1). A surgery report was not available for 1 dog.

Biopsy specimens were obtained from the duodenum and jejunum in 10 dogs, the duodenum alone in 6 dogs, and the jejunum alone in 1 dog (1 sample was obtained from each location). It was not always specified in the surgical reports why certain areas of intestine were chosen for biopsy. Intestinal thickening, when recorded, was diffuse throughout the small intestine.

Intestinal lymphangiectasia was determined to be histologically mild in 6 dogs, moderate in 6 dogs, and severe in 5 dogs. There was no apparent difference in the severity of lymphangiectasia between the duodenal and jejunal samples. Six dogs also had lymphangiitis, which was neutrophilic in 3, granulomatous in 2, and eosinophilic in 1. Three of the dogs with lymphangiitis had severe IL, and 3 had mild IL.

Concurrent inflammatory cell infiltrates were recognized in 15 of 17 surgical biopsy specimens. Inflammation was lymphocytic-plasmacytic in 7 dogs, lymphocytic in 3 dogs, eosinophilic in 3 dogs, mixed lymphocytic-plasmacytic and eosinophilic in 1 dog, and plasmacytic in 1 dog. Four dogs had severe inflammation, 3 had moderate inflammation, and 6 had mild inflammation. In the remaining 2 dogs, the resident population of inflammatory cells (lymphocytes and plasma cells) was within reference range limits. Of these 2 dogs without considerable inflammation, 1 had severe IL, and 1 had mild IL. In all 4 dogs with severe inflammation, lymphangiectasia was mild.

Crypt ectasia was evident in 5 dogs. Three of these dogs had severe IL, 1 had moderate IL, and 1 had mild IL. Two of the dogs with lymphocytic-plasmacytic inflammation also had lipogranulomas. One of these dogs had severe lymphangiectasia, and 1 had mild lymphangiectasia.

Of the 3 dogs that were normoalbuminemic, 1 had mild IL, and 2 had moderate IL. Of the dogs that were normoglobulinemic, 2 had mild IL, 4 had moderate IL, and 1 had severe IL. Of the dogs that were normocholesterolemic, 3 had mild IL, 4 had moderate IL, and 1 had severe IL. Of the dogs with lymphocyte counts within reference range, 1 had mild IL, 3 had moderate IL, and 2 had severe IL. Of these 4 variables, the severity of hypoalbuminemia appeared to offer the best correlation with histologic severity of lymphangiectasia.

Of the 5 dogs with severe IL, 4 had abdominal ultrasonographic examinations performed. No abnormalities were found in 1 of these 4 dogs. Three dogs had evidence of small intestinal wall thickening, and 1 of these dogs also had a hyperechoic small intestinal mucosal layer and indistinct small intestinal wall layers. Of the 8 dogs with mild or moderate IL that had ultrasound examinations performed, abnormalities were found in 5 dogs, which included small intestinal wall thickening, hyperechoic small intestinal mucosal layer, and small intestinal wall corrugation.

Of the 4 (of 16) dogs with a grossly thickened small intestine described at surgery, 1 had severe IL, 2 had moderate IL, and 1 had mild IL (the dog for which there was no surgical report had severe IL). Two of these 4 dogs also had ultrasonographic evidence of small intestinal wall thickening. Of the other 2 dogs with a grossly thickened small intestine, 1 did not undergo ultrasonographic examination.
Three dogs had concurrent neoplastic diseases not involving the gastrointestinal tract, including mammary ductal carcinoma, malignant fibrous histiocytoma, and adrenal adenoma. Of 7 dogs that were euthanized, 3 were euthanized within 2 days of surgery because of complications (1 dog developed seizures and presumed pulmonary thromboembolism, and 1 dog had peritonitis and an open abdomen) or poor prognosis (1). One dog was euthanatized 13 months after diagnosis because of recurrent ascites. Three dogs had development or progression of another disease process: 1 developed neurologic disease 3 months after diagnosis, 1 had progression of malignant fibrous histiocytoma < 1 month after diagnosis, and 1 had a mesenteric torsion 3.3 months after diagnosis.

Discussion

We found that the most common clinical signs of IL included gastrointestinal tract abnormalities (ie, diarrhea, vomiting), anorexia, lethargy, and weight loss. These results are consistent with other reports of IL in dogs, but the incidence of diarrhea was higher than reported previously. Intestinal lymphangiectasia has been cited as 1 of the protein-losing enteropathies for which lethargy and weight loss are the predominant clinical signs.

Other than mild increases in ALT, ALP, and AST, hypoaalbuminemia was the only consistently abnormal finding in the serum biochemical profile. Other clinicopathologic findings previously reported in dogs with IL include hypocholesterolemia, hypoglobulinemia, and lymphocytopenia. These abnormalities were detected in 5 of 13, 6 of 13, and 8 of 14 dogs, respectively. Therefore, we conclude that hypoglobulinemia, hypocholesterolemia, and lymphocytopenia are not always present, even with histologic evidence of moderate to severe IL, and that a diagnosis of IL should not be excluded in the absence of these abnormalities. Consistent with our findings, there is 1 previous report of a German Shepherd Dog with intractable diarrhea that had IL and a lymphocyte count and serum protein concentration within reference range. It was presumed in this case that the rate of protein synthesis was greater than the rate of protein loss, although this hypothesis was not substantiated.

None of the dogs with serum albumin concentrations within reference range had severe IL, and most but not all dogs that had lymphocyte counts within reference range, normocholesterolemia, and normoglobulinemia had only mild or moderate lymphatic dilatation. Therefore, we conclude that the severity of clinicopathologic abnormalities, particularly hypoaalbuminemia, correlates with the severity of IL in most dogs.

In dogs with hypoaalbuminemia and normoglobulinemia (4/12), concurrent inflammatory infiltrates in the intestinal wall may stimulate increased globulin production in the face of excessive protein loss via the gastrointestinal tract. Of these dogs, 1 had severe inflammation, 1 had moderate inflammation, and 2 had mild inflammation. This number of dogs was insufficient to conclude whether the inflammation affects globulin concentration in dogs with concurrent IL.

Other disorders that should be excluded in dogs with hypoaalbuminemia and normoglobulinemia include protein-losing nephropathy and liver disease. In the dogs of our study, notable glomerular disease was unlikely, because only 2 dogs had trace or 1+ proteinuria. Liver disease could not be definitively ruled out in the 4 dogs that were hypoalbuminemic and normoglobulinemic, because liver function tests (ie, serum bile acid concentration) and liver biopsy were not performed. However, none of the 4 dogs had abnormal ALT activity or total serum bilirubin concentration, and BUN was within reference range or slightly higher. Blood ammonia concentrations were measured in 2 of these dogs and results were within reference range. One of these dogs had hypocholesterolemia, but this was likely attributable to IL.

The dog that had melena did not have a CBC or serum biochemical analysis performed at our hospital. Therefore, this dog’s laboratory values were not included in the means calculated for albumin and globulin; results of these 2 variables would have been difficult to interpret in this dog, because both IL and blood loss would be contributing to their decline.

Hypocalcemia can result from fat malabsorption attributable to formation of calcium-fatty acid complexes in the intestinal lumen. In addition, hypocalcemia may result from vitamin D malabsorption; it is important to recognize this abnormality because hypocalcemia may result in tetany or weakness, although neither of these clinical signs were observed in any of the dogs in our study. Abnormalities in magnesium concentration may also develop with IL, however, serum magnesium was not measured in any of our dogs.

Coagulation profiles were performed in 12 dogs and abnormalities were found in only 1 dog. Coagulopathies may develop in dogs with protein-losing enteropathy (PLE) because of decreased absorption of vitamin K. Hypercoagulability resulting in thrombosis may be a concern in dogs with protein-losing enteropathy. The proposed mechanisms include loss of antithrombin III (ATIII), hyperaggregation of platelets, increases in fibrinogen, and vascular damage as well as other imbalances in coagulation/anticoagulation, which have been documented in humans. Measures of hypercoagulability such as fibrinogen, D-dimers, and ATIII were not performed in the dogs of this study; therefore, it is possible that they were at increased risk of thrombosis although there was no clinical evidence of thrombus formation.

To the authors’ knowledge, there are no published data on the imaging findings in dogs with IL. Most (12/17) dogs in our study had ultrasonography performed prior to exploratory laparotomy. Abdominal radiography was performed in only 6 dogs. Ascites was noticed on physical examination in 5 of the dogs in which radiography was not performed; the decision not to perform abdominal radiography may have been based on this finding.
Abdominal radiographic abnormalities (ie, ascites) were not specific for dogs with IL. In contrast, there were many ultrasonographic findings suggestive of intestinal disease. Abnormal findings included intestinal wall thickening (> 3.0 mm), hyperchogenicity of the small intestinal mucosal layer, small intestinal wall corrugation, indistinct small intestinal wall layering, and small intestinal hypermotility. Peritoneal effusions were observed in 7 of 12 dogs in which ultrasonography was performed. The small intestinal abnormalities were subtle and best seen using high frequency transducers (> 7.5 MHz). Although no intestinal masses were evident, small intestinal wall thickening and loss of normal layering can also be seen with neoplasia, although intestinal masses were not observed in any dogs in this study. Although these ultrasonographic findings are not specific for IL, this information (along with clinicopathologic abnormalities) supports the pursuit of surgery to obtain intestinal biopsies.

Ultrasonographic abnormalities did not appear to correlate with the severity of IL in this group of dogs. However, most dogs with moderate or severe IL had abnormalities on ultrasonographic examination, whereas those with mild IL had fewer abnormalities. Thickening of the small intestine (detected during surgery) did not always correlate with thickening of the small intestine on ultrasonographic examination. Only 1 dog had a thickened small intestine at surgery and not ultrasonographically, whereas 4 dogs had a thickened small intestine noted on the ultrasound report but not on the surgical report.

Crypt ectasia was evident in 2 dogs. Severe crypt dilation compresses the base of the adjacent villi, which may lead to lymphatic obstruction. Although there is 1 report of abnormal deep crypts in dogs with IL, this was thought to be attributable to increased enterocyte turnover. The association of crypt ectasia and IL was recently reported in a case series in which dilated crypts were evident in 6 dogs with PLE, 2 of which had lymphangiectasia.

It has been reported that lipogranulomas may be associated with IL and are usually detected in the mesenteric lymphatics or intestinal serosa along the mesenteric border. It is believed that lipogranulomas result from granulomatous reactions to lymph leakage from ruptured lymphatic vessels. In our study, there was no mention in the surgical reports of grossly visible lipogranulomas. On histologic examination of the small intestinal biopsy specimens, intramural lipogranulomas were evident in 2 dogs.

Two dogs in our study were euthanatized because of life-threatening complications that developed shortly after surgery. The risk for thrombosis in dogs with PLE may be exacerbated by surgical manipulation (and subsequent damage) of blood vessels. In addition, dogs with IL may be at a greater risk for the development of leakage from intestinal biopsy sites, because samples are obtained from diseased tissue. Although it was suggested in a previous report that hypoalbuminemia did not affect wound healing, it has been recognized that recovery from intestinal biopsy may be complicated in dogs with PLE.

Submucosal dilation of lymphatics is a criterion for diagnosis of IL; therefore, full-thickness intestinal biopsies may be required to substantiate the diagnosis. However, clinical case descriptions in the veterinary literature appear to report equal involvement of mucosal and submucosal lymphatic vessels in this disease. And 1 recent report included 7 dogs in which lymphangiectasia was diagnosed by collection of mucosal biopsy specimens via endoscopy. Additional study is necessary to determine the value of obtaining only mucosal biopsy specimens in the diagnosis of IL.

We conclude that IL is a heterogeneous disease and that most dogs with mild to moderate IL are not as severely panhypoproteinemic, hypocholesterolemic, and lymphocytopenic as has been previously reported. Ultrasonographic findings (ie, intestinal wall thickening, hyperchogenicity of the small intestinal mucosal layer, small intestinal wall corrugation, indistinct small intestinal wall layering, and small intestinal hypermotility) provide evidence of intestinal disease, but these changes are not specific enough to differentiate IL from other gastrointestinal tract disorders, nor are they predictive of severity of disease. Histologic evaluation is necessary to confirm the diagnosis of IL. However, other diagnostic procedures may be designed in the future to help screen for IL prior to performing biopsy procedures.

References


