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Focal Intestinal Lipogranulomatous Lymphangitis in 6 Dogs (2008–2011)

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Background: Lipogranulomatous lymphangitis is inflammation of the intestinal lymphatic vessels and surrounding tissues caused by chronic leakage of lipid-laden chyle. Grossly, lipogranulomas are typically disseminated small masses on the serosa and surrounding lymphatic vessels and consist of epithelioid macrophages, multinucleated giant cells, and cholesterol. Lipogranulomatous lymphangitis is occasionally seen in patients with lymphangiectasia and protein-losing enteropathy (PLE).

Objectives: To characterize the historical features, clinical signs, treatment, histopathology, and outcome of dogs with focal lipogranulomatous lymphangitis.

Animals: Six dogs with ultrasonographic evidence of focal, regional small intestinal masses, often with involvement of the adjacent mesentery, and a diagnosis of focal lipogranulomatous lymphangitis based on histopathology of biopsied masses.

Results: The median age of dogs was 6.9 years (range 3–10 years). All dogs had total protein, globulin, and albumin concentrations within the reference range at initial presentation and had intestinal masses identified on abdominal ultrasound examination. Histopathologic evaluation of lesions identified severe mural and mesenteric lipogranulomatous lymphangitis. Lymphangiectasia was noted in 5 cases and only in sections within the mass-like lesion; tissue without lipogranulomas had minimal lymphangiectasia, suggesting a localized phenomenon. Postoperative outcomes ranged from remission of clinical signs with no subsequent treatment for 10–12 months in 2 dogs, postoperative management with medical and nutritional management in 3 dogs, and no outcome for 1 case.

Conclusions and Clinical Importance: This case series describes a unique mass-like manifestation of intestinal lipogranulomatous lymphangitis and should be considered as a possible differential diagnosis in dogs with an intestinal mass.

Key words: Abdominal pain; Intestinal mass; Lymphangiectasia; Ultrasound.

Intestinal lipogranulomatous lymphangitis, first described in 1973, is inflammation of the lymphatic vessels and surrounding tissues within the intestinal wall, serosa, and mesentery. Lipogranulomas typically appear grossly as discrete 5–10 mm nodules along the serosal and mesenteric lymphatics.[1] The nodules are composed predominantly of epithelioid macrophages and multinucleated giant cells with phagocytized and extracellular lipid and cholesterol clefts. Lipogranulomatous lymphangitis is thought to be a response to chronic leakage of lipid-rich chyle and rupture of lymphatic vessels with subsequent foreign body-type reaction, and can occur concurrently with lymphangiectasia and hypoproteinemia.[1,2]

Abbreviations:

PLE	protein-losing enteropathy
SC	subcutaneous
LF	low fat

Intestinal lymphangiectasia occurs in several species, including dogs and humans.[1] It is defined as marked dilatation and dysfunction of intestinal lymphatic vessels, including lacteals and serosal lymphatic vessels.[1,3] Intestinal lymphangiectasia is often associated with protein-losing enteropathy (PLE) and serum biochemistry findings include panhypoproteinemia, hypocholesterolemia, and lymphopenia. The main ultrasonographic findings of lymphangiectasia are hyperechoic mucosal striations in the small intestine resulting from reflection of ultrasound waves on the dilated lacteals, but little information is available on the ultrasonographic findings associated with large lipogranulomas.[4,5]

Although lipogranulomatous lymphangitis has been well described as a disseminated intestinal disease, there is only a single case report of focal disease in the veterinary literature.[5] In the current report, we examine a series of cases with focal lesions characteristic of lipogranulomatous lymphangitis. Six biopsy assessments from 6 unrelated dogs with similar histopathologic lesions of regional lipogranulomatous lymphangitis were made at the University of Pennsylvania. The objective of this report is to describe the clinical signs, presenting physical examination findings, ultrasound images, surgical lesions, pathologic findings, and clinical outcomes of these 6 cases of focal lymphatic intestinal disease.

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Materials and Methods

Criteria for Selection of Cases

Cases were included if they had ultrasonographic evidence of a small intestinal circumferential thickening, mural mass, or mesenteric mass that subsequently was surgically removed by laparotomy and resection and anastomosis surgery or mesenteric mass removal. The histopathologic findings included focal to regional lipogranulomatous lymphangitis within the serosa, mucosa, mesentery, or some combination of these. All animals were client-owned dogs living within the greater Philadelphia area and were assessed at one of the following specialty and emergency clinics: Veterinary Specialty and Emergency Center in Langhorne, PA; Veterinary Referral Center and Emergency Service in Malvern, PA; Veterinary Specialty Center of Delaware in New Castle, DE; and the Center of Animal Referral and Emergency Services in Langhorne, PA.

Procedures

Information available from the 6 cases included signalment, presenting complaint, abdominal imaging findings, and clinicians' differential diagnoses. Clinical laboratory results and long-term outcomes were available for 5 of 6 cases; 1 case was lost to follow-up. Tissues were fixed in 10% buffered formalin, processed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (H&E). All biopsy specimens were assessed by a board-certified pathologist (ACD).

Results

Signalment

Breeds represented were as follows: Bichon Frise (Case 1), Harrier (Case 2), Bloodhound (Case 3), Maltese mix (case 4), Münsterländer (case 5), and Standard Poodle (case 6). Four dogs were neutered males and 2 were spayed females. The median age at the time of diagnosis was 6.9 years (range 3–10 years).

History and Presenting Clinical Signs

Histories of all patients included at least 3 weeks of signs of intra-abdominal disease, including abdominal pain, diarrhea, vomiting, and weight loss. The longest history was that of dog 5, which had a 2-year history of intermittent abdominal pain and a previous endoscopic biopsy diagnosis of inflammatory bowel disease. Presumably unrelated histories included dog bite wounds in the abdominal area 1 year before presentation in dog 1, *Dirofilaria immitis* diagnosis and treatment at a young age in dog 2, and intermittent anal sacculitis in dog 6. The most frequent presenting complaint was vomiting (4/6), followed by intermittent abdominal pain (3/6), weight loss (2/6), diarrhea (2/6), hypersalivation (1/6), decreased appetite (1/6), and stretching with head and thorax lower to the ground and abdomen and caudal end higher (1/6).

Clinicopathologic Data

Complete blood count and serum biochemistry results were available for 5/6 dogs, and all analytes were within normal reference ranges. Specifically, total protein, albumin, globulin, and cholesterol concentrations, as well as lymphocyte counts, were within the reference range at initial presentation in all cases. Two of the 6 dogs had urinalyses and sediment evaluation performed and no clinically relevant findings were reported.

Diagnostic Imaging

Abdominal ultrasound examination was performed in all 6 dogs; detailed reports were available for 5/6 dogs and the other had a short, concise report. Four of the 6 dogs had circumferential muscularis thickening of the jejunum or ileum with no loss of wall layering; 1 dog had a multilobulated, 3.0×2.0 cm, hypoechoic mass within the mesentery between caudal jejunal loops; and 1 dog had a midjejunal, nonobstructive, asymmetrical, $1.39 \times 0.52 \times 3.75$ cm, serosal mass with 4.07 cm of inspissated, hyperechoic omentum surrounding the area. One dog with muscularis thickening also had a focal isoechoic to mildly hyperechoic intramural mass that caused loss of wall layering. The circumferential thickening ranged from 0.7 cm to 1.0 cm and the distinct intestinal to mesenteric masses adjacent to the small intestine ranged in size from 3×2 cm to 4.07 cm in diameter. Other areas examined were considered normal other than a small, singular hypoechoic nodule in the spleen of 2/6 dogs. Based on ultrasonography, the tentative clinical diagnosis most often was neoplasia, followed by inflammation and lymphangiectasia. Preoperative, 3-view, thoracic radiographs were performed in 3/6 dogs; no evidence of metastastic disease was present. Preoperative thoracic radiographs and postoperative thoracic radiographs were performed in dog 5: the preoperative radiographs were within normal limits and postoperative radiographs were performed after development of a cough and displayed a progressive, alveolar pattern in the left cranial lung lobe, right middle lung lobe, and right cranial lung lobe, which was interpreted to be bronchopneumonia presumably caused by postoperative aspiration. Two dogs had abdominal radiographs performed before the ultrasound examination and both had gas-filled dilated loops of small intestine and dog 2 had an area of increased soft tissue or fluid opacity in the mesentery.

Surgery

Resection and anastomosis surgery was performed in all 6 dogs. No gastrointestinal lesions, including masses or dilated lymphatic vessels, were macroscopically evident other than in the section removed. Biopsies were also collected from normal-appearing intestine in 1 dog. All dogs recovered from anesthesia without complications other than dog 5 that developed and recovered from aforementioned aspiration pneumonia.

Histopathologic Findings

Histopathologic lesions were similar in all 6 dogs and affected the distal jejunum or ileum. The wall of

the small intestine was markedly expanded by inflammation, dilated lymphatics, and fibrosis. The inflammation within and surrounding lymphatic vessels of the submucosa, muscularis, and serosa consisted of epithelioid and foamy macrophages, variable numbers of multinucleated giant cells, neutrophils, and lymphoplasmacytic infiltrates. Most dogs (5/6) also exhibited lacteals dilated within the villi (Fig 1A), regions of necrosis (4/6), and acicular cholesterol clefts within the granulomas (4/6), some of which were phagocytized by macrophages (Fig 1B). Dogs 1, 2, 4, and 5 did not have any lesions within the marginal sections of the mass; dog 5 also had stomach and duodenal full-thickness biopsies without any clinically relevant lesions. Dog 3 had lymphatic lesions extending to the distal margin of the jejunal mass; however, the proximal margin did not have any lesions. The lymphatic lesions extended to both orad and aborad margins in dog 6. All dogs were diagnosed with regional lipogranulomatous lymphangitis.

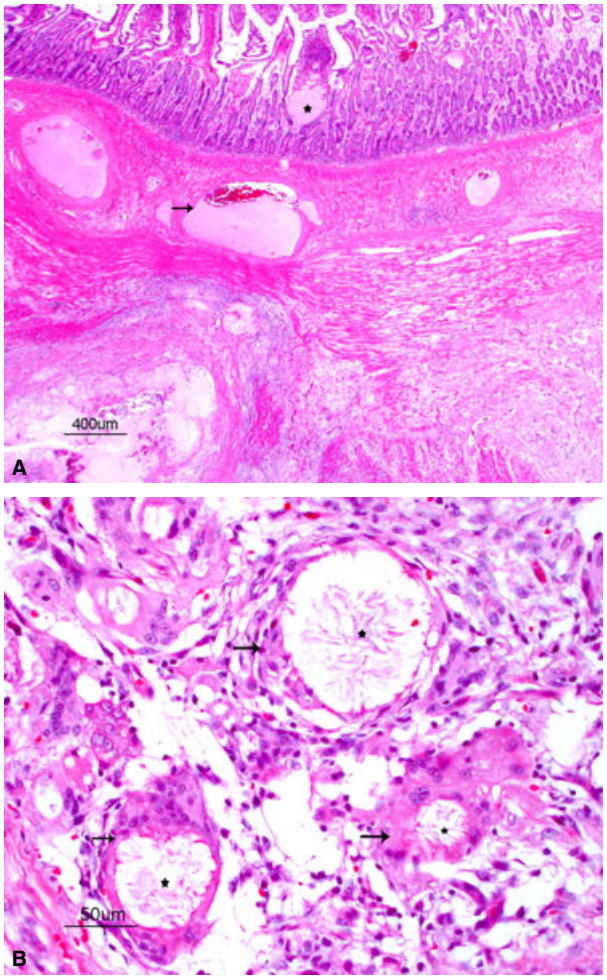

Fig 1. (**A**) The wall of the small intestine is markedly thickened by inflammation, fibrosis, lymphatic dilatation, and necrosis. The lacteals (star) in affected regions and lymphatic vessels within the submucosa and muscularis (arrow) are ectatic. H & E. 20×; Bar = 400 μm. (**B**) Higher magnification of the inflamed region of muscularis. The inflammation consists of a mixture of neutrophils, lymphocytes, and plasma cells, as well as numerous epithelioid macrophages and multinucleated giant cells (arrow), which surround and engulf cholesterol clefts (star). H & E. 200×; Bar = 50 μm.

Clinical Outcome

All dogs were discharged from the hospitals where surgery was performed, and clinical outcome was available for 5 of the 6 dogs; case 3 was lost to follow-up. Three of the 5 dogs (dogs 1, 2, and 5) had long-term remission, defined as at least 11 months, of clinical signs with surgical intervention only. Dog 1 received no postoperative nutritional or medical management. Two episodes of abnormal behavior, interpreted as abdominal pain by the owner (telephone communication), were reported but not confirmed by the veterinarian. Dog 2 had an acute episode of vomiting 11 months after surgery, recovered with treatment consisting of fluids administered SC and famotidine, and then was lost to follow-up. It remains uncertain if the single vomiting episode was associated with recurrence of lipogranulomatous lymphangitis. Dog 5 was doing well for more than 1 year after surgery with several repeated normal abdominal ultrasound examinations. However, 3 years after surgery, the dog developed severe abdominal pain, and an abdominal ultrasound examination showed thickening of the small intestinal, cecal and colonic walls, a focal intestinal wall mass (1.8 × 3.4 cm) at the ileocecocolic junction, and mild peritoneal effusion. The dog's serum albumin concentration at that time ranged from 1.7 to 2.2 g/dL (reference range, 2.3–4.0 g/dL). The owner elected to not pursue surgery and the dog showed improvement with orally administered prednisolone for 8 months, at which time its appetite decreased. An additional ultrasound examination did not identify the previous ileocecocolic mass, but the dog was euthanized based on progressive nonspecific gastrointestinal signs and poor quality of life.

The remaining 2 dogs (dogs 4 and 6) did not have long-term remissions from their clinical signs. Both dogs were started on dietary management, medical management, or both within 2 weeks of surgery. Dog 4 had recurrence of clinical signs within 2 weeks of surgery. An abdominal ultrasound examination showed intestinal mural thickening distal to the surgical site. Surgery was not performed, and medical and nutritional management was initiated: Royal Canin Veterinary diet canine Gastrointestinal Low Fat LF dry dog food,[a] prednisolone, azathioprine, and psyllium. Dog 6 has been maintained since surgery on a diet of boiled chicken, low-fat cottage cheese, pasta, and a variety of vegetables. The dog continues to have abdominal ultrasound examinations performed biannually with no recurrence of disease for 3 years postoperatively. Four of the 6 affected dogs are known to be alive at the time of writing.

Discussion

This case series describes a focal manifestation of intestinal lipogranulomatous lymphangitis as a differential

diagnosis in dogs with abdominal mass and normal hematology and serum biochemistry findings. There are several key differences in the clinical characteristics of these cases compared with previously reported cases of intestinal lymphangiectasia and lipogranulomatous lymphangitis. We report lesions that are focal to regional and form localized masses as opposed to disseminated small nodules. There was no laboratory evidence of PLE on serum biochemistry at presentation, and no medical management was needed for months to years after surgical removal of the masses in most cases. Some similarities of focal lipogranulomatous lymphangitis with lymphangiectasia compared to diffuse intestinal lymphangiectasia were also noted: both diseases affect primarily older animals, presented with vomiting, weight loss, and diarrhea, and both have unclear pathogeneses.[1–3] In this case series, some of the animals affected with a localized lesion progressed to develop clinical signs and laboratory findings consistent with PLE, indicating the possibility of disease progression.

Of diagnostic relevance, the specificity of abdominal ultrasound examination for the diagnosis of lipogranulomatous lymphangitis remains unclear. Changes in echogenicity seen with classic forms of lymphangiectasia are seen with other inflammatory diseases.[4] The lesions reported here are isoechoic to mildly hyperechoic or surrounded by a rim of hyperechogenicity. These findings differ from those of intestinal neoplasms, specifically adenocarcinoma and lymphoma, which are hypoechoic.[6] Therefore, the imaging features may be useful in prioritizing inflammation over neoplasia.

Given the complexity of the pathogenesis of inflammatory bowel disease, lymphangiectasia, and lymphangitis, the underlying cause for the focal nature of the lesions described in this case series remains unclear. Lymphangitis can be seen with several intestinal diseases, including Crohn's disease in humans, in which lesions are more commonly found in portions of the intestinal tract in which lymphoid follicles are most numerous, and infrequently in regions with the poorest lymphatic supply.[7,8] The lesions seen in our case series occurred in the distal small intestine, with 5/6 in the distal jejunum and 1 in the ileum, a site of numerous Peyer's patches. Interestingly, the single case report of focal lymphangiectasia described a 7-year-old West Highland White Terrier with no laboratory abnormalities and a 10-cm-long circumferential mass within the ileum.[5]

In conclusion, we report a case series of dogs with large distal small intestinal masses found during abdominal ultrasound examination, diagnosed by biopsy with focal lipogranulomatous lymphangitis, and with no evidence of PLE. The limitations of this study include the relatively small sample size, incomplete follow-up data in some cases, and lack of biopsies from other intestinal sites. Complete surgical excision of the lesion, as well as full-thickness intestinal biopsies from sites distant from the mass, should be performed to confirm the focal nature of the lesion. Focal lipogranulomatous lymphangitis is uncommon in dogs, but should be included as a differential diagnosis for an intestinal mural mass or mural thickening.

Footnote

[a] Royal Canin, St. Charles, MO, USA

Acknowledgment

Conflict of Interest Declaration: Authors disclose no conflict of interest.

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