NOTE *Clinical Pathology*

Histiocytic Ulcerative Colitis in a French bulldog

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ABSTRACT. A 9-month-old French bulldog was referred for signs of chronic large bowel diarrhea. The dog had an increased frequency of defecation, tenesmus and hematochezia. Flexible colonoscopy showed hyperemia, irregularities and ulcerations with multifocal hemorrhages in the mucosa from the descending colon to the proximal rectum. Multiple colonic biopsies were characterized by infiltrations of PAS positive histiocytes in the lamina propria. A diagnosis of histiocytic ulcerative colitis (HUC) was made, and the animal showed only minimal improvement, although it was treated with nutritional and medical therapies. This is the second case of HUC in French bulldog, a breed which has ancestral relations to Boxer dogs.

KEY WORDS: French bulldog, histiocytic ulcerative colitis, PAS-positive histiocyte.

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Histiocytic ulcerative colitis (HUC) is a form of inflammatory bowel diseases and occurs most frequently in Boxer dogs [2–4]. HUC may be a distinct disease in this breed, and the histopathologic changes differ from those reported in other breeds [3]. The disease is characterized by histiocytic infiltration of the lamina propria [5]. The onset of clinical signs occurs predominantly in young dog, before 2 years of age. The clinical signs of HUC may include diarrhea, hematochezia, increased frequency of defecation, tenesmus, excessive mucus, and occasionally weight loss or inappetence in severe cases [2, 7]. HUC is confirmed by colonic biopsy, which reveals infiltration of periodic-acid Schiff (PAS)-positive macrophages in the lamina propria of colonic tissue [11]. Clinical signs frequently fail to improve with medical therapy (e.g. immunosuppressive drugs, anti-inflammatory agents, antimicrobial drugs and dietary modification), therefore a prognosis is generally considered to be guarded to poor [4], although remission and clinical improvement have been reported in early or mild cases [2, 5, 6, 11, 13]. This paper describes one case of HUC in a French bulldog.

A 9-month-old, intact female French bulldog weighing 10.7 kg was referred with a five month history of large bowel diarrhea. The diarrhea was characterized by an increased frequency of defecation and occasional tenesmus. The feces were soft in consistency and contained variable amounts of fresh blood and mucus. There was no history of vomiting or weight loss. Previous treatment with dietary modifications had not resolved clinical signs. Physical examination findings were within normal limits. Results of a complete blood count, serum chemistry and salt fecal flotation were unremarkable, with the exception of mild leucocytosis (14,100/μl). Serum trypsin-like immunoreactivity was normal. Organisms identified from fecal culture included *Kluyvera ascorbata*, *Escherichia coli* and *Proteus mirabilis*. Radiographic examinations by barium enema and double contrast study were performed initially. The barium enema examination was unremarkable, but the double contrast study revealed mild mucosal irregularities from the distal descending colon to the proximal rectum (Fig. 1). Colonoscopy was performed to evaluate the extent of the radiographic abnormality using an electronic video endoscope system for animal (FUJINON VETERINARY ENDOSCOPE SYSTEM EV-250PE; Fuji Photo Optical, Saitama, Japan). It revealed hyperemia, irregularities and ulcerations with multifocal hemorrhages in the mucosa of the distal descending colon and proximal rectum (Fig. 2). Multiple colonic biopsies were obtained from the edge of ulceration to avoid the artificial changes and obtain samples accurately, and histopathologic examinations were carried out using sections stained with hematoxylin and eosin (HE) and PAS. Infectious pathogenic bacteria and neoplastic lesions were not evident by histology, however the colonic lamina propria was infiltrated with a large number of histio-

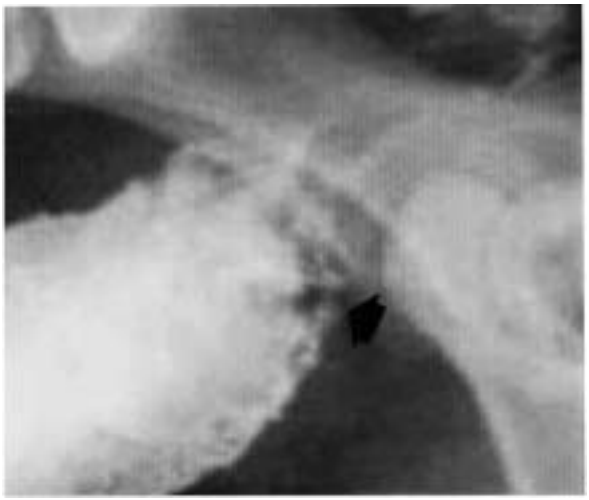

Fig. 1. Double contrast study, right lateral view. There are mild mucosal irregularities from the distal descending colon to the proximal rectum (arrow).

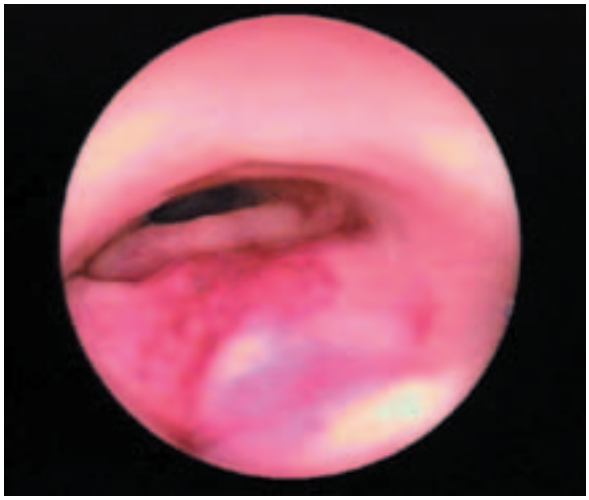

Fig. 2. Finding of the flexible colonoscopy. The hyperemia, irregularities and ulcerations with multifocal hemorrhages in the mucosa of the distal descending colon.

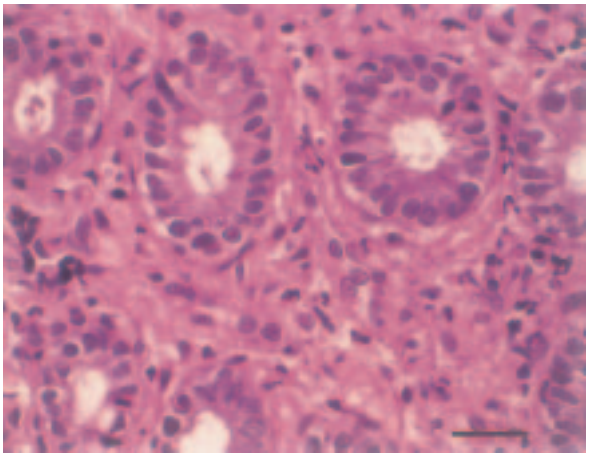

Fig. 4. Photomicrograph of the colonic biopsy sample. The colonic lamina propria was infiltrated with a large number of histiocytes. Neutrophils and lymphocytes are also present. HE stain, Bar=25 μm.

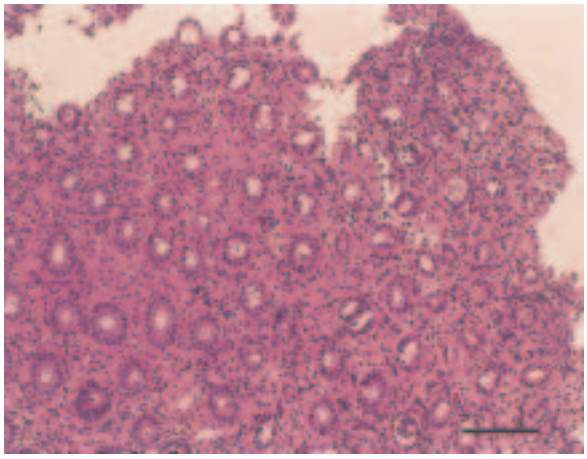

Fig. 3. Photomicrograph of the colonic biopsy sample. Thickened lamina propria due to marked cellular infiltration. HE stain, Bar=100 μm.

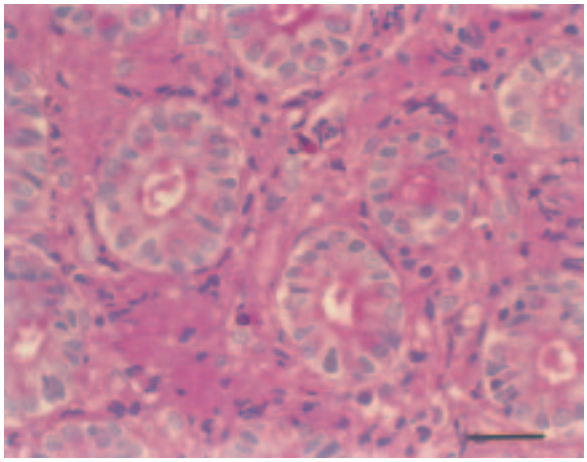

Fig. 5. Photomicrograph of the colonic biopsy sample. The cytoplasm of histiocytes in the colonic lamina propria is positive for PAS. PAS stain, Bar=25 μm.

cytes which have a fine granulated cytoplasm on HE sections (Figs. 3 and 4). The cytoplasm of these histiocytes was positively stained with PAS (Fig. 5). Neutrophils and lymphocytes were also present in the lamina propria. Based on these findings, a pathologic diagnosis of HUC was made.

Treatment was initiated with metronidazole (15 mg/kg body weight, PO BID), prednisolone (1 mg/kg body weight, PO BID) and bismuth subnitrate (0.1 g/kg body weight, PO divided twice a daily) and the diet was changed to a highly digestible food (WALTHAM® Selected Protein Diet™; Master Foods, Kanagawa, Japan), but clinical signs were not resolved. Therefore another treatment was initiated with salazosulfapyridine (15 mg/kg body weight, PO TID) and prednisolone (continued same doses). The hematochezia was resolved, but the fecal consistency remained soft and the animal had continued increased frequency of defecation. Despite continued salazosulfapyridine and prednisolone therapy, the dog had persistent hematochezia for 2 weeks. The owners declined further treatment, and therapy was discontinued. At the time of last follow-up, approximately 3 months after therapy was discontinued, the dog had persistent the clinical signs of large bowel diarrhea.

HUC has been recognized as a form of severe large bowel diseases particularly in Boxer dogs. HUC in Boxer dogs was first described in the U.S.A. in 1965 [13]. Subsequently, there have been reports of the disease in various countries [1, 3, 6–9]. HUC has been reported in other breeds including a French bulldog [12], a Mastiff, an Alaskan mal-

amute, and a Doberman pinscher [10]. These additional case reports have shown that HUC can occur in dogs other than Boxer dogs. In this case report, the onset of the disorder was at 4 months of age, and the clinical signs consisted of increased frequency of defecation, tenesmus and hematochezia. The response to medical therapy was poor, and the clinical course was similar to many previous reports. The non-boxer breeds may respond more favorably to therapy than Boxer dogs and some authors have noted that mildly affected dogs may respond to therapy if treated at an early stage [2, 5, 6, 11, 13] , however in our report the dog did not respond well to therapy. The dog was diagnosed at 9 months of age and it may have been too late to initiate therapy, although the prognosis of the French bulldog with HUC may be considered to be guarded to poor as same in many cases of Boxer dogs [2, 5].

Various presumptions have been made about the etiology of this disease. An inherited predisposition, infectious factors and environmental factors have all been suggested [2, 3]. Environmental factors such as emotional stress or behavioral aberrations were not reported by the owner, therefore factors other than environment may have been more important. HUC was described as a granulomatous colitis resembling Whipple's disease in man and Johne's disease in ruminant [3, 5, 8, 13]. In Whipple's disease, intracellular bacteria are evident in macrophages, and John's disease is known as a granulomatous enteritis caused by *Mycobacterium paratuberculosis*. However, it is not proved that infectious factors have a causative role in HUC at the present [4]. In our case, bacteria isolated from the fecal culture were considered part of the normal microflora in the gastrointestinal tract, and other infectious agents that infiltrate macrophages, such as fungi or mycobacteria, were not found in the histological section. The occurrence of HUC mainly in Boxer dogs suggests a strong genetic component in its development. A genetic predisposition could not be proved in this case, however this is the second case of HUC in a French bulldog, a breed which has ancestral relations to Boxer dogs. Therefore, it was considered that genetic factors may be important in the pathogenesis of HUC in Boxer dogs and a related breed.

In conclusion, it is important to recognize that HUC can be encountered in breeds other than Boxer dogs. Furthermore, HUC should be considered in the differential diagnosis of a French bulldog which has clinical signs of chronic large bowel diarrhea at an early age. Colonoscopy and biopsy are useful in establishing a definitive diagnosis at an early stage of the disease.

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