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Treatment of Lymphocytic Gastritis with Cyclosporine in a Cat

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Abstract : A 7-year-old spayed female domestic shorthair cat was referred for chronic intermittent vomiting. The frequency of vomiting increased recently, and the cat showed anorexia at presentation. There were no remarkable abnormalities on the blood analyses and diagnostic imaging. However, the endoscopic examination revealed focal erosions of the gastric body mucosa, and subsequent multiple biopsies were obtained. Histopathologic examination indicated mild to moderate lymphocytic gastritis. The vomiting was completely disappeared 7 days after the administration with prednisolone (PDS). However, because of side effects caused by the long-term PDS administration, cyclosporine was added on the prescription with tapered dose of PDS. The dog's condition improved with continued cyclosporine treatment, and no further vomiting and anorexia episodes have been noted. This case describes the successful management with administration of cyclosporine in feline lymphocytic gastritis.

Key words **:** endoscopy, feline, lymphocytic gastritis, prednisolone.

Introduction

Lymphocytic gastritis is a described histopathological entity, characterized by the mature T-lymphocytic infiltration of superficial and foveolar gastric epithelium (4,5,9). Endoscopically, there are enlarged rugal folds bearing nodular erosions principally involving the body of the stomach, though in some cases of histological lymphocytic gastritis, the endoscopic appearances may be normal (4).

The mainstay of treatment for feline lymphocytic gastritis has been prednisolone (PDS), whereas chlorambucil is an alternative drug that can be used to allow a reduction in PDS dose (12). However, chlorambucil has a modest increased risk of secondary malignancy, bone marrow suppression, and neurotoxicity (1). Cyclosporine has been described as an effective alternative to immunotherapy without serious side effects. In cats, several studies and anecdotal reports have described its efficacy and apparent safety, and the use of cyclosporine is gaining acceptance for treatment in a variety of immune-compromised diseases, including inflammatory bowel disease (IBD) (3), atopic dermatitis (7), granulomatous folliculitis and furunculosis (9), and granulomatous sebaceous adenitis (13). However, treatment with cyclosporine has not been reported in cats with lymphocytic gastritis. Herein, we describe the treatment with cyclosporine in a domestic shorthair cat with lymphocytic gastritis.

Case

A 7-year-old, spayed female domestic shorthair cat weighing 4 kg was referred with a 3-month history of chronic intermittent vomiting. The frequency of vomiting increased recently, and the cat had anorexia. At presentation, no abnormal findings in physical examination were shown. Blood analyses showed no remarkable abnormalities. There were also no abnormalities on the survey radiographs and abdominal ultrasonographs. Endoscopic examination, however, revealed focal erosions, and edematous and thickened gastric body mucosa, without evidences of ulceration, foreign bodies, or neoplasia (Fig 1). Histopathologic examination of gastric biopsies showed mild to moderate infiltrates of lymphocytes within the lamina propria (Fig 2). No abnormal bacterial populations were noted, and these findings were suggestive of lymphocytic gastritis.

Initial treatment consisted of 1 mg/kg of prednisolone (q12h,

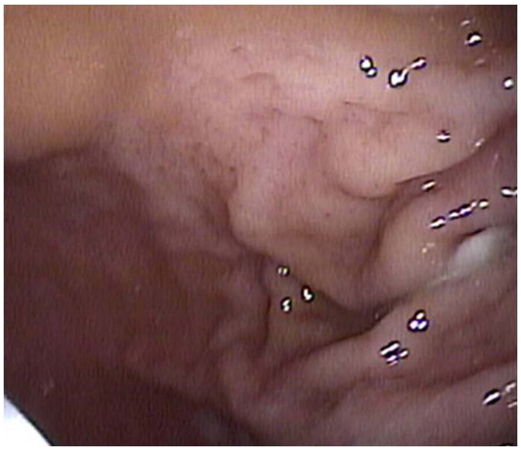

Fig 1. An endoscopic view of the gastric body wall obtained from a cat with lymphocytic gastritis. Edematous and thickened gastric mucosa with focal erosions is visible.

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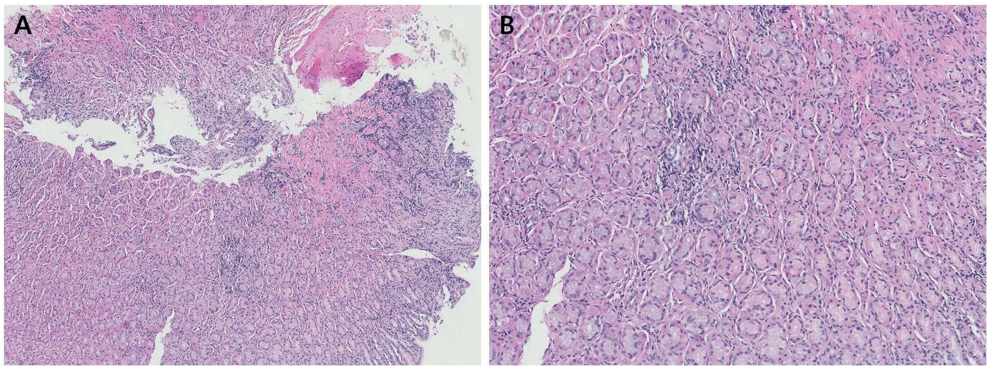

Fig 2. Microscopic images of biopsy from the gastric mucosa typical of the fundic region. There are lymphocytic infiltrations within the lamina propria of the gastric mucosa (H&E stain; A, × 50; B, × 100).

PO; Solondo®, Yuhan Co., Korea), 0.5 mg/kg of famotidine (q12h, PO; Famotidine®, Nelson, Korea), 10 mg/kg of ursodeoxycholic acid (q12h, PO; Ursa®, Daewoong, Korea), and 1 mg/kg of maropitant citrate (q24h, PO; Cerenia®, Pfizer, USA) with the prescription of hypoallergenic diet. The vomiting and inappetance disappeared, and there was no relapse when administration of maropitant citrate was stopped for evaluation of the effect of PDS without antiemetics. At three weeks after the PDS therapy, the dose was reduced to 0.75 mg/kg twice a day then symptoms were relapsed. On relapse, the patient was re-treated with PDS at the initial dose. The cat did not show vomiting on this dose of PDS for two months, however, the serum biochemistry revealed an increase in the activities of alkaline phosphatase (ALP) and alanine transaminase (AST). In addition, the owner complained about polyuria, polydipsia, poor hair condition and focal alopecia around the pad resulting from chronic administration of PDS. Then, oral administration of cyclosporine (5 mg/kg, q24h; CIPOL-N, Chong Kun Dang, Korea) was added to prescription for the patient.

The dose of PDS was tapered to 0.75 mg/kg (q12h, PO) 2 weeks after the initiation of cyclosporine administrations. There was no relapse of vomiting and inappetance. At that time, serum cyclosporine concentration was 265 ng/mL. The PDS administration was discontinued 8 weeks after cyclosporine therapy, and there were no relapsed vomiting. During the monotherapy with cyclosporine, she did not vomit or show any clinical signs associated with lymphocytic gastritis or side effects of treatment with cyclosporine.

Discussion

In this case, the cat was diagnosed with lymphocytic gastritis based on endoscopic and histopathologic findings. Although the cat responded well to the treatment with PDS, PDS was tapered due to adverse effects. Alternatively, cyclosporine, known to have a larger margin of safety compared to chlorambucil, was prescribed leading to successful results without any side effects.

Cyclosporine acts as an immune suppressant by interfering with production of interleukin (IL) from helper T-lymphocytes, making killer T cells not be armed and thus non-effective (2). In lymphocytic gastritis, an immune-mediated disease characterized by infiltration of mature T-lymphocytes within gastric epithelium, cyclosporine may be more effective than other immune suppressants in that it has specific effect on T-cells. However, several side effects caused by cyclosporine have been reported, including gastrointestinal upset (diarrhea, vomiting and anorexia), increased hair growth, gingival hyperplasia, and flare of latent viral infection (9). Moreover, the therapeutic dose of cyclosporine in the management of feline IBD has not been well established. Oral administration of cyclosporine has been successful to treat furunculosis, sebaceous adenitis, and alopecia areata at a dosage of 5 mg/kg once a day (6,7). Therefore, the dose of administered cyclosporine in our case was determined based on immunosuppressive dose used in previous studies. Fortunately, in the present case, the cat responded well to treatment with cyclosporine alone, and no side effects associated with use of cyclosporine were found with 265 ng/mL of blood concentration of cyclosporine. However, further studies will be necessary to establish the standard protocol for the treatment of lymphocytic gastritis or IBD in cats. Lymphocytic gastritis is a histopathologic diagnosis, which is a special type of chronic gastritis characterized by extensive infiltration of intraepithelial lymphocytes (3,4). The underlying basis of the immunologic response of gastritis is rarely identified, although lymphocytic gastritis is common in dogs and cats. However, it is usually attributed to bacterial or dietary antigen-associated immune response (12). In the present case, dietary allergen-induced lymphocytic gastritis was ruled out because the cat had been eating hypoallergenic diet over 2 months.

One study demonstrated that dogs with lymphoplasmacytic gastritis of undetermined etiology showed concurrent activation of pro-inflammatory cytokines (IFN-α, IL-1β, and IL-8) and immunomodulatory cytokine (IL-10) (10). Regarding the central role of IL-10 in modulating proinflammatory responses and gastrointestinal inflammation, a complex interaction in immunologic environment in the gastrointestinal

tract cannot avoid active inflammation by antigen exposure, which subsequently results in induction of immune intolerance (12), then lymphocytic gastritis may be developed. Meanwhile, IBD is a group of idiopathic chronic gastrointestinal disorders, characterized by infiltration in the intestinal tract by inflammatory cells, associated with persistent or recurrent clinical signs of a gastrointestinal disease of an undetermined cause (3). Lymphocytic-plasmacytic gastritis, the most common type of chronic gastritis in cats, is often associated with lymphocytic-plasmacytic enteritis, which is the most commonly reported with IBD (5). However, in our case, an apparent cause associated with the infiltrations of lymphocytes could not determine.

Our case report has several limitations. Immunophenotyping for expression of CD3 and CD79a is required to clarify the lineage of the infiltrating population and differentiate small cell lymphoma from lymphocytic plasmacytic enteritis (8). In addition, full thickness biopsies through laparoscopy or laparotomy should be performed when the diagnostic inconsistency in differentiation between IBD and small cell lymphosarcoma exists (11). Other limitation was that there was no serial monitoring on the change in gastric mucosa by using gastroendoscopy after the treatment with cyclosporine was initiated. In the present case, however, a full thickness biopsy through invasive laparotomy was not performed because the cat fortunately responded well to immunosuppressive therapy. Serial evaluation on the gastric mucosa could not be performed owing to the refusal of the owner.

In conclusion, this case study describes the successful application of cyclosporine as a monotherapy in a cat with lymphocytic gastritis. The findings reported here indicate that cyclosporine may be an effective alternative to other immune suppressants, which have been used for management of feline lymphocytic gastritis. Further population-based studies will be necessary to verify the exact effect of cyclosporine in feline lymphocytic gastritis.

Acknowledgments

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고양이 림프구성 위염에서 싸이클로스포린을 이용한 치료 증례

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요 약 : 7세 중성화된 암컷 고양이가 3개월 동안 지속된 간헐적인 구토 증상으로 진료 의뢰되었다. 혈액 검사와 진단 영상학적 검사에서 비정상적인 소견은 관찰되지 않았다. 내시경 검사에서 위 동체 점막에 국소적인 미란이 관찰되었고, 해당 병변들에 대한 조직병리학적 검사를 통해 림프구성 위염으로 진단하였다. 프레드니솔론 투약 7일 후에 구토 및 식욕 부진 증상은 소실되었지만, 장기간 투약에 의한 부작용 발생 때문에 프레드니솔론 대신에 싸이클로스포린을 처방하였다. 환자의 상태는 개선되었고, 구토와 식욕부진은 더 이상 관찰되지 않았다. 본보는 만성 구토를 보이는 고양이 림프구성 위염에 있어 싸이클로스포린은 치료 약물로 적용 가능함을 시사한다.

주요어 : 내시경, 고양이, 림프구성 위염, 프레드니솔론