Case Report

Successful management of feline gastrointestinal eosinophilic sclerosing fibroplasia with mycophenolate mofetil and prednisolone following surgical resection in a cat

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Abstract

A 1-year-old castrated male Ragdoll who showed a series of vomiting and had reduced appetite presented to a local animal hospital. Hyperthermia and tachypnea were observed in physical examination, and leukocytosis was detected in hematological examination. Abdominal ultrasonography revealed an intramural mass with irregular echogenicity extending from the pylorus to the duodenum and loss of intestinal wall layer with regional lymph node enlargement. After exploratory laparotomy for biopsy and symptomatic alleviation, histopathological evaluation revealed densely infiltrated eosinophils within the branching and anastomosing trabecular pattern of collagen by several spindle-shaped cells. Finally, the patient was diagnosed with feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF). Since the pathogenesis of FGESF is known to be abnormal immune response, immune-modulatory treatment was recommended following surgical resection. According to previous studies, mycophenolate mofetil (MMF) is known to potentiate the efficacy of prednisolone (PDS) for treating other immune mediate disease. Therefore, combination therapy was conducted in this patient. There has been no evidence of recurrence since the initiation of immunotherapy. This case showed the importance of accurate diagnosis as well as suggested one of therapeutic options for veterinary clinicians in medical treatment following resection of FGESF.

Keywords: Feline Gastrointestinal Eosinophilic Sclerosing Fibroplasia, Immunosuppressants, Mycophenolate mofetil, Prednisolone

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Introduction

Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF), which is an emerging disease, is characterized by unique eosinophilic masses within the intramural part of the gastrointestinal (GI) tract (Criag *et al*., 2009). Although the complete mechanism of FGESF remains unclear, there have been several reports suggesting that the cause of FGESF is abnormal inflammatory response to antigens (Criag *et al*., 2009; Echstrand *et al*., 2013). Therefore, immunosuppressive therapy with surgical excision showed a better prognosis than other treatment methods (Criag *et al*., 2009; Linton *et al*., 2015). The ages of patients diagnosed with FGESF range from 14 weeks to 16 years, and the median age ± standard deviation is 8.8 ± 4.4 years. The commonly reported clinical signs of FGESF include chronic vomiting, diarrhea, weight loss, lethargy, excessive grooming, and coughing (Linton *et al*., 2015).

As there are no unique clinicopathological feature of FGESF, it is challenging to rule out other neoplastic diseases (Weissman *et al*., 2013). Considering that FGESF presents as an ulcerated mural mass having neoplastic appearance, it can be easily confused with malignant tumor and sometimes make the owner abort appropriate treatment (Criag *et al*., 2009; Weissman *et al*., 2013). Despite these difficulties, FGESF is diagnosed by histological examination. Histologically, the major lesions of FGESF are featured with infiltration of eosinophils and fibroplasia of the lesion comprising branching and anastomosing trabeculae of dense collagen and spindle-shaped cells (Linton *et al*., 2015).

As a prodrug of mycophenolic acid, mycophenolate mofetil (MMF) is known to affect inosine-5′-monophosphate dehydrogenase and inhibit T- and B-lymphocyte proliferation (Allison and Eugui, 2005). Although MMF is one of the immunosuppressants, it does not have adverse effects regarding nephrotoxicity and fibrogenicity (Allison and Eugui, 2005). Therefore, it is used to treat immune mediated diseases in both human and companion animal and several researches revealed satisfactory efficacy (Ackermann *et al*., 2017). Especially in cats, there are several studies that MMF was selected to treat immune-mediated disorders along with corticosteroids for potentiating efficacy and minimal adverse effect (Lenore *et al*., 2011; Tamura *et al*., 2020). Considering that the etiology of FGESF is abnormal immune response, MMF can be a good treatment option for adjuvant therapy with corticosteroids.

Case Report

A 1-year-old castrated male Ragdoll presented to a local animal hospital. The chief complaint was reduced appetite after vomiting thrice within a day. On physical examination, hyperthermia (41.7℃) and tachypnea (>60/min) were noted. Although SpO2 was not measured, RBCs (6.87×10^{12}/L) and MCV (50.6 fL) were within normal range. Complete blood count showed significant elevation of WBC (33.2×10^{9}/L) with monocytosis (3.2×10^{9}/L) and neutrophilia (27×10^{9}/L). However, hypereosinophilia was not detected. Serum chemistry evaluation showed significant elevation of total bilirubin (TBIL; 1.9 umol/L) and alanine transaminase (ALT; 519 U/L) levels. All other values were within the normal ranges.

Radiographic evaluation of the abdomen revealed a mass effect in the upper and middle abdomen (Fig 1 A). Displacement of the stomach to the left side of the abdomen was observed, with unclear margin of the gastroduodenal junction. Abdominal ultrasonographic examination confirmed the long mass located in the lumen of the GI tract from the pyloric region of the stomach to the proximal part of the duodenum (Fig 1 B, C). The thickness of wall layer of the gastric pylorus (reference interval [RI]; 1.9-2.4mm) and duodenum (RI; 2-2.4mm) was remarkably enlarged to 4.4mm and to 6.9mm respectively. And the wall layering the inside of the GI tract was lost. Furthermore, the enlargement of lymph node around the jejunum (30.03 × 9.78, reference interval [RI], length: 11.4–39.0 mm, diameter: 2.8–7.2 mm) and lymph node of pancreatic duodenum (14.69 × 8.99, RI, length: 6.6–13.0 mm, diameter: 3.6–6.2 mm) were detected without morphological changes.

Exploratory laparotomy was performed for excisional biopsy and symptomatic alleviation caused by the mass (Fig 2). Considering the difficulties in approaching the intestinal lesion, partial excision was performed around the pyloric sphincter muscle. Histopathological examination revealed transmural proliferation with branching and anastomosing trabeculae of dense collagen with eosinophils and neutrophils (Fig 3 A, B). Furthermore, a relatively significant number of large spindle-shaped cells were observed within the collagen fibers. Bacteria were not observed. Considering these findings, the patient was diagnosed with FGESF.

After diagnosis of FGESF, fenbendazole (250 mg/cat P.O. once), amoxicillin–clavulanate (12.5 mg/kg P.O. twice daily), doxycycline (5 mg/kg P.O. twice daily), and omeprazole (1 mg/kg P.O. once daily) were administered with prednisolone (PDS) (2.0 mg/kg P.O. twice daily) for 7 days. After a week, MMF (10 mg/kg P.O. once daily) was also prescribed as an immunomodulatory drug for 7 days. Clinical signs including vomiting and reduced appetite started to improve within 2 weeks, with decreased sectional size from 15.77mm × 16.55mm to 13.93mm × 9.93mm of the lesion on ultrasonographic examination (Fig 1 D, E). Moreover, the sizes of the jejunal and pancreaticoduodenal lymph nodes decreased from 30.03mm × 9.78mm to 23.42mm × 7.72mm and 14.69mm × 8.89mm to 10.55mm × 8.79mm respectively. Other serum chemistry levels also returned within the normal ranges and recurrence of the clinical signs was not observed. PDS dosage was gradually tapered to 0.5 mg/kg P.O. twice daily over 12 weeks, and there was no sign of recurrence at the time of writing (over 6 months).

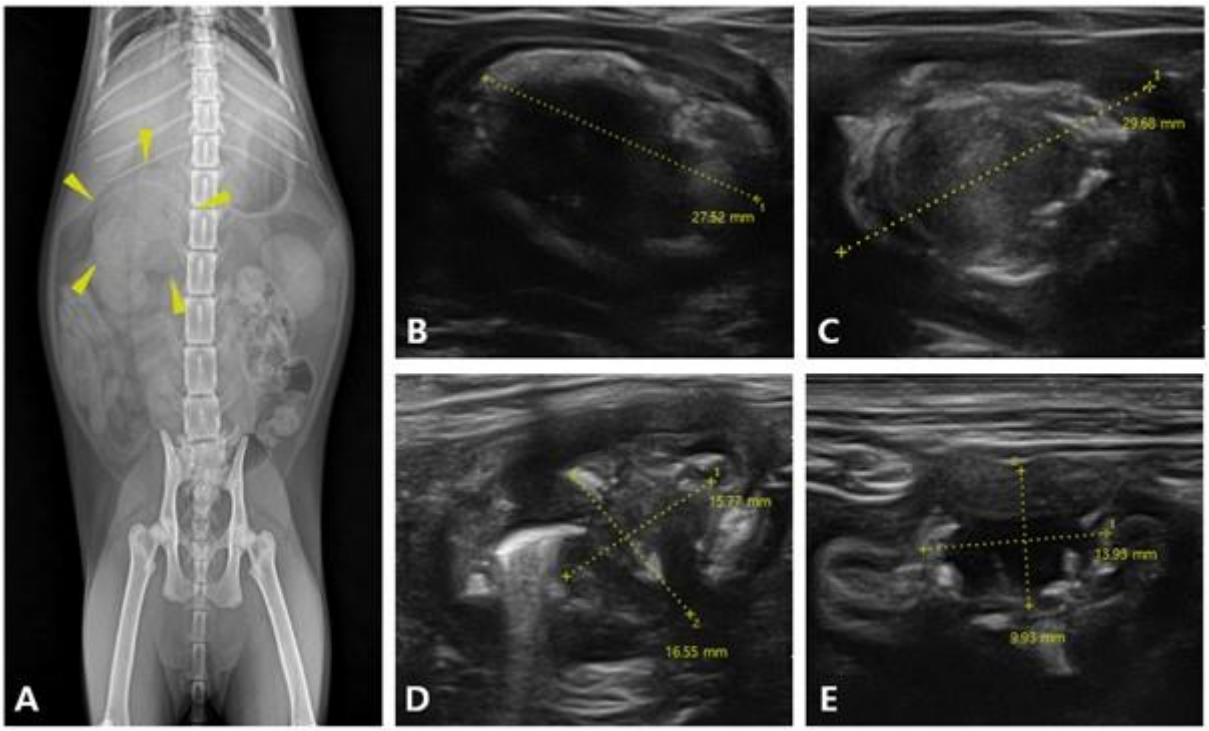

Figure 1 Radiographic and ultrasonographic evaulation of the lesion before and after treatment.
(A) A single mass with soft tissue opacity was observed between the pylorus and duodenum. The mass had a length of two lumbar vertebrae bodies (yellow arrow head). (B) Ill-defined hypoechoic mass with relatively clear hyperechoic margination in the stomach. The length of the mass is indicated by the dotted line (27.52 mm). (C) Rough and hypoechoic mass with irregular hyperechoic border in the duodenum. The length of the mass is indicated by the dotted line (29.88 mm). Both (B) and (C) were measured at the first presentation and the mucosal and submucosal layers are lost, and the external muscle layer seems hyperplastic in both of ultrasonographic images. (D) Remaining mass with heterogenous echogenicity after partial resection of mass at pylorus. The length and diameter of the mass are indicated by the dotted line (15.77 mm × 16.55 mm). (E) Mass with decreased size 2 weeks after medical treatment. The length and diameter of the mass are indicated by the dotted line (13.99mm × 9.93mm)

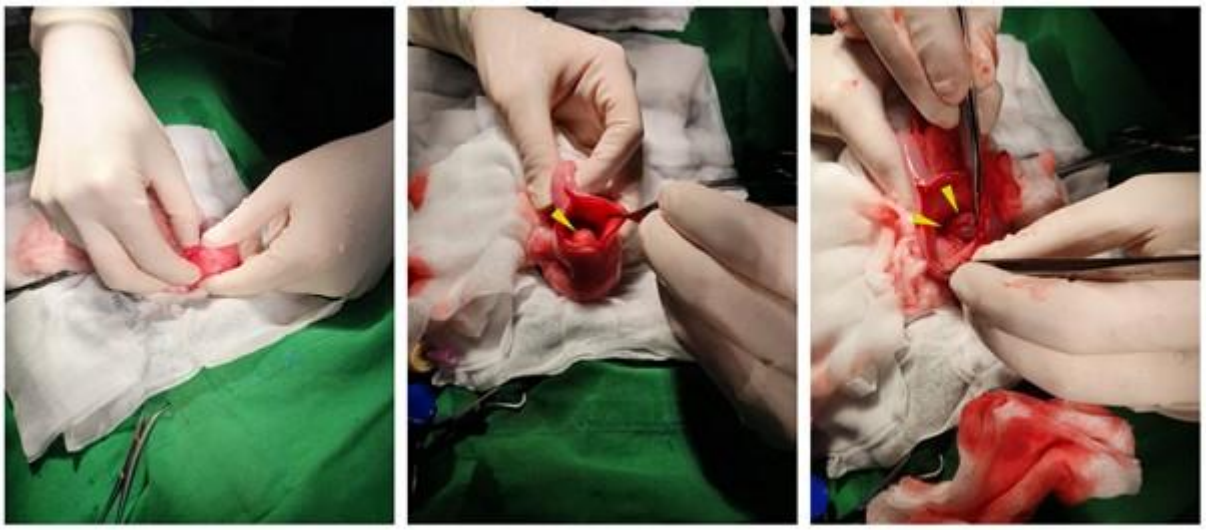

Figure 2 Macroscopic finding on exploratory laparotomy
We confirmed that the lesion was located through gastric pylorus and proximal duodenum on exploratory laparotomy (yellow arrow head). The lesion was round and soft mass with clear margination.

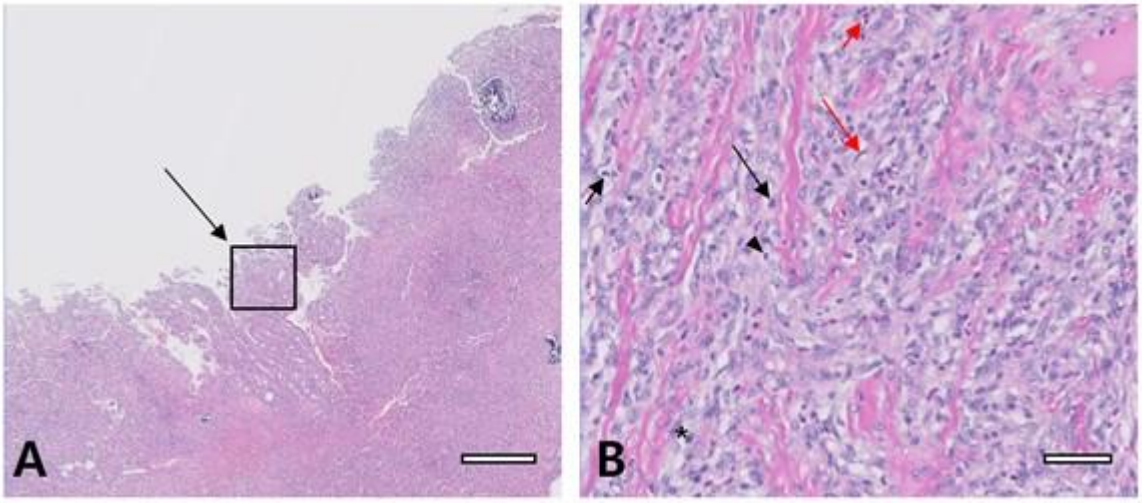

Figure 3 Histologic evaluation of a mass from the stomach using hematoxylin and eosin staining.
(A) Photomicrographs of the mass from partial gastric excision. The resected mass comprises several eosinophils and some neutrophils with collagen fibers. Hematoxylin and eosin staining (×50. White bar, 500um). (B) With dense cellular population of large spindle-shaped cells (long red arrow), there are dense infiltrations of numerous inflammatory cells including eosinophils (short red arrow), mast cells (long black arrow), neutrophils (short black arrow), lymphocytes (black arrow head), and plasma cells (asterisk) within the lesion. Furthermore, small foci of dystrophic mineralization admixture are seen. Hematoxylin and eosin staining (×400. White bar, 50um)

Discussion

Although the etiology of FGESF remains unknown, large fibroblasts which shares some similar morphological features with neoplastic mesenchymal cells are remarkably embedded in the lesion and these reactive fibroblasts produce a considerable amount of collagen (Criag *et al*., 2009). For instance, fibrosarcoma and osteosarcoma are featured with patterned extracellular matrix where mesenchymal cells have malignant nuclear and nucleolar changes (Augsburger *et al*., 2017). These features make a diagnosis challenging. Moreover, intestinal sclerosing mast cell tumor also can be mistaken for FGESF because mast cells within the stromal collagen, severe infiltration of eosinophils can be observed (Halsey *et al*., 2010). However, in this patient, mitotic figures and other malignant cells were not observed and numerous inflammatory cells such as eosinophils, lymphocytes, and plasma cells in the sclerosing lesion were detected, which is consistent with most FGESF cases (Criag *et al*., 2009; Thieme *et al*., 2019). These features could help well-trained pathologic specialist diagnose easily. This case suggests that aggressive diagnostic method is worth performing when a young cat with alimentary mass visits to the animal hospital.

According to several previous studies, which recommended a combination protocol including physical resection and immunotherapy, we prescribed the patient with PDS and MMF following the excision of the mass in the GI tract (Criag *et al*., 2009; Linton *et al*., 2015; Thieme *et al*., 2019). MMF was chosen because it can control immune system by inhibiting T- and B-lymphocytes with much less side effects such as myelotoxicity and hepatotoxicity compared to other immunosuppressants (Viviano, 2013). Other study has suggested that MMF can be used as a second-line immunotherapeutic drug with glucocorticoids (Ackermann *et al*., 2017). Moreover, it can be a relatively safe immunosuppressive drug option with minimal adverse effects such as diarrhea or weight loss in cats (Slovak and Villarino, 2017). Therefore, MMF was selected to reduce the immune-mediated reaction in this case of FGESF. Consequently, drug treatment following the surgery showed significant effectiveness to decrease the size of unresected mass with further improvement of clinical signs. Therefore, this case showed the potential efficacy of MMF with PDS for FGESF after surgical resection.

This case reported the importance of aggressive diagnostic method to differentiate from other neoplastic diseases and successful treatment using MMF with PDS following surgical treatment. As FGESF has relatively good prognosis with appropriate treatment compared to neoplastic diseases, it should be considered as a differential diagnosis in cats with alimentary intramural masses. We hope that our diagnostic method and therapeutic plan can help provide better treatment options to veterinary clinicians and the owner of cats for treating FGESF.

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