Case Report

Mycotic pyogranulomatous enteritis in a German shepherd: imaging diagnosis and treatment

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Abstract

A five-year old, intact male, German Shepherd dog was presented to the hospital due to a history of depression, anorexia, vomiting and diarrhea. Physical examination revealed moderate emaciation and showed mild abdominal pain when Palpation. Abdominal radiographs and ultrasounds showed the distension of the small bowel loop due to partial obstruction of the colon by mural concentric thickening. Computed tomography (CT) scan showed an homogeneous, soft tissue mass with asymmetric thickening of the cecum traversing the colonic wall. Pre-operative blood profiles indicated normocytic normochromic mild anemia, hypoalbuminemia and mild hyperglobulinemia. Intestinal resection and anastomosis at the distal ileum to the proximal descending colon were done. The cross section of the intestinal mass was of irregular shape with firm consistency and loss of wall layering. Biopsy was obtained by full thickness enterectomy which revealed severe chronic mycotic pyogranulomatous enteritis. After staining with Periodic acid-Schiff (PAS) and Gomori's methenamine silver (GMS), histopathologic results indicated the intra-lesion septate branching hyphae of fungal element. There was no evidence of recurrent intestinal mass at the surgical site through ultrasonographic examination at 5 month-post-operative monitoring.

Keywords: CT scan, German Shepherd, mycotic pyogranulomatous enteritis, radiograph, ultrasound

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Introduction

Granulomatous enteritis is significant disease that is the cause of morbidity and mortality in immunosuppressed patients (Lamps *et al*., 2014). It is described as an inflammation of the intestinal tract that is predominantly infiltrated by macrophages and/or multinucleated giant cells. The inflammation of the intestinal tract may be diffuse and/or form organized granulomas (Amarnath *et al*., 2021). The development of granulomatous inflammation is usually due to foreign material (e.g. migrating foreign bodies, suture material) or invasive pathogens (e.g. bacteria, fungi) that could not be eliminated. The immune system attempts to engulf these pathogens leading to granulomatous formation (Song *et al*., 2011). In some cases, the causes of this abnormality cannot be investigated, however, immune mediation is also suspected (Song *et al*., 2011). Granulomatous enteritis has been reported in dogs (Lewis, 1995), cats (Duchaussoy *et al*., 2015; Leal *et al*., 2017), horses (Lindberg, 1984) and pigs (Machuca *et al*., 2012). In dogs, this abnormality occurs in any sex, breed and age (Amarnath *et al*., 2021). The pathogenesis is still unknown. Similar to granulomatous inflammation, the cause of granulomatous enteritis can be classified into 3 types including infectious (e.g., bacteria, fungi, algae, oomycetes, and viruses), foreign bodies (e.g., migrating foreign body, suture material, etc.) and idiopathic. Since this abnormality is significant disease in immunocompromised patients and it has never been reported in Thailand, the aim of this report is to provide an overview of the diagnosis process of granulomatous enteritis, on the clinical presentation, imaging features, blood profiles, surgical treatment and histological findings in a granulomatous enteritis affected German Shepherd dog.

Case report

A five-year old, 27-kilogram, intact male, German shepherd dog was presented to the Small Animal Teaching Hospital, Faculty of Veterinary Science, Chulalongkorn University during January 2021 with a history of intermittent vomiting, lethargy and weight loss. On the day of presentation, general physical examination revealed normal heart sound and lung sound, normal hydration status, strong femoral pulse without pulse deficit but, when abdominal palpation was performed, the dogs showed signs of abdominal discomfort. CBC and serum biochemistry profile indicated normocytic normochromic mild anemia, hypoalbuminemia and mild hyperglobulinemia (Table 1). Then, abdominal radiographs on ventrodorsal and lateral projections were taken (Fig. 1A and 1B) using a digital x-ray (ETL®, GE healthcare, Beijing, China). The radiographs showed focal small intestinal ileus with multiple small pieces of foreign body indicating chronic partial obstruction of intestinal loops and loss of serosal detail (Fig. 1). The dog was referred for further diagnosis by transabdominal ultrasound scanned using a 7 MHz, linear transducer (Logiq P6®, GE healthcare, Seoul, Korea) on ventrodorsal position. The ultrasound revealed transmural thickening and loss of wall layering (Fig. 1C) and intestinal ileus at the cranioventral abdomen. Therefore, a computed tomography (CT scan) was performed in this case as a protocol of pre-operative planning. A CT scan was done by prone position with the head pointing into a 4-slice CT scanner (Toshiba Astetion, USA). The dog was scanned, both for scout and pre-contrast studies, using the following parameters: a low-pass filter, 2.0 mm slice thickness, collimator pitch at 0.531, matrix of 512 x 512, peak kilovoltage of 120 kVp, and 150 mA, in which the region of interest covered the whole abdominal area. As soon as the pre- contrast scan was completed, 300 mgI/kg of (Omnipaque™, GE healthcare, Shanghai, China), was intravenously administered through the right cephalic vein and the scan was then repeated as a post-contrast enhanced study. All data was saved as Digital and Communication in Medicine (DICOM) files and view by OsiriX® software (OsiriX®, Pixmeo SARL, Geneva, Switzerland) with abdominal window; window width (WW: 40 Hounsfield unit, HU) and window level (WL: 380 HU). A CT scan showed conspicuous circumferential wall thickening of the cecum to the transverse colon with homogeneous attenuation and luminal narrowing (Fig. 2A and B). Subsequently, the dog was scheduled for surgical excision of the intestinal mass using intestinal resection and end to end anastomosis technique. Prior to anesthesia, the dog was fasted for 8 hrs. Premedication was done using an IV administration of 0.3 mg/kg of morphine sulfate pentahydrate (Morphine sulfate®, M & N manufacturing, Samutprakarn, Thailand), followed by an induction of anesthesia using slow IV administration of 4 mg/kg propofol (Propofol-®Lipuro, B.Braun Melsugen AG, Melsungen, Germany). After endotracheal intubation, the dog was maintained in generalized anesthesia with 2% isoflurane (AERRANE®, Baxter Healthcare Corporation, Deerfield, USA) in 100% oxygen. The metronidazole sodium chloride (Metrogyl®, Sagent Pharmaceuticals, Schaumburg, USA) at 15 mg/kg intravenously was given as surgical antibiotic prophylaxis. The excisional biopsy and excision of the intestinal mass was done by removal of the distal ileum to the distal transverse colon (Fig. 3A). A cross section of the intestinal mass revealed focal granulomatous enteritis with a loss of bowel layering (Fig. 3B). The biopsy sample was submitted for further histopathological investigation. Histopathological findings of the cross section of the intestinal mass revealed mild hyperplasia of mucosal epithelium and increased chronic granulation tissue in the muscular layer. Severe multifocal to coalescing pyogranuloma invaded from serosal to muscular layer and submucosa on dense fibrous stoma. Each pyogranuloma consisted of necrosis, accumulation of segmented neutrophils, macrophages, lymphocytes and plasma cells, mixed with loosely interlacing bundles of collagen fibers and reactive fibroblasts (Fig. 4A). The Presentation of intralesional septate branching hyphae of the fungal element was shown by positive staining of Periodic acid-Schiff (PAS) (Fig. 4B) and Gomori's methenamine silver (GMS) (Fig. 4C). The result indicated mycotic pyogranulomatous enteritis for which the differential diagnosis was *Pythiosis* or *Basidiobolomycosis spp*. Nevertheless, the fecal culture was negative for any fungi growth. In addition,

bacterial culture and sensitivity testing were done from the intestine. The results showed numerous *b-hemolytic streptococcus spp*. and *Escherichia coli*. After surgery, anti-inflammatory drugs, using 4 mg/kg carprofen (Rimadyl®, Zoetis LLC, NE, USA) were given for 3 consecutive days while post-operative antibiotics were continued for 14 days. At 5 months post-operative ultrasonographic findings were unremarkable. The dog was well and had increased in body weight from 27.0 to 35.9 kg. Physical examination was normal. The repeat complete blood count, serum biochemistry and transabdominal ultrasound were within referent range.

Table 1 Hematology and serum biochemistry of the dog.

Parameter	Result	Reference Range
Complete Blood Count		
WBC (x 10^3/uL)	9.32	(6.0-17.0)
Neutrophils (%)	74.8	(60-77)
Absolute (x 10^3/uL)	(6971)	(3000-15,000)
Band	0	(0-3)
Absolute (x 10^3/uL)	0	(0-510)
Lymphocyte (%)	11.5	(12-30)
Absolute (x 10^3/uL)	(1071)	(1000-4800)
Monocytes (%)	6.3	(3-10)
Absolute (x 10^3/uL)	(587)	(180-1350)
Eosinophils (%)	7.4	(2-10)
Absolute (x 10^3/uL)	(689)	(1000-1250)
HCT (%)	31.2	(37.0-55.0)
HGB (g/dl)	11.6	(12.0-18.0)
RBC (x10^6/uL)	4.95	(5.5-8.5)
Platelets (x10^3/uL)	218	(200-500)
Blood parasite detected from buffy coat smear	Not found	
Blood Chemistry		
BUN (mg/dL)	15.6	(7-26)
Creatinine (mg/dL)	1.1	(0.6-1.4)
ALT (U/L)	24	(4-91)
Alkaline Phosphatase (U/L)	17	(3-60)
Total Protein (g/dL)	6.8	(5.8-7.9)
Albumin (g/dL)	2.2	(2.6-4)
Globulin (g/dL)	4.6	

WBC = white blood cells; HCT = Hematocrit; HGB = hemoglobin; RBC = red blood cells; BUN = blood urea nitrogen; ALT = alanine aminotransferase
RBC = red blood cells; MCV = mean cell volume; MCH = mean cell haemoglobin; MCHC = mean cell haemoglobin concentration; RDW = red blood cell distribution width; WBC = white blood cells; BUN = blood urea nitrogen; ALT = alanine aminotransferase; AST = aspartate aminotransferase; ALP = alkaline phosphatase; GGT = g-glutamyl transpeptidase

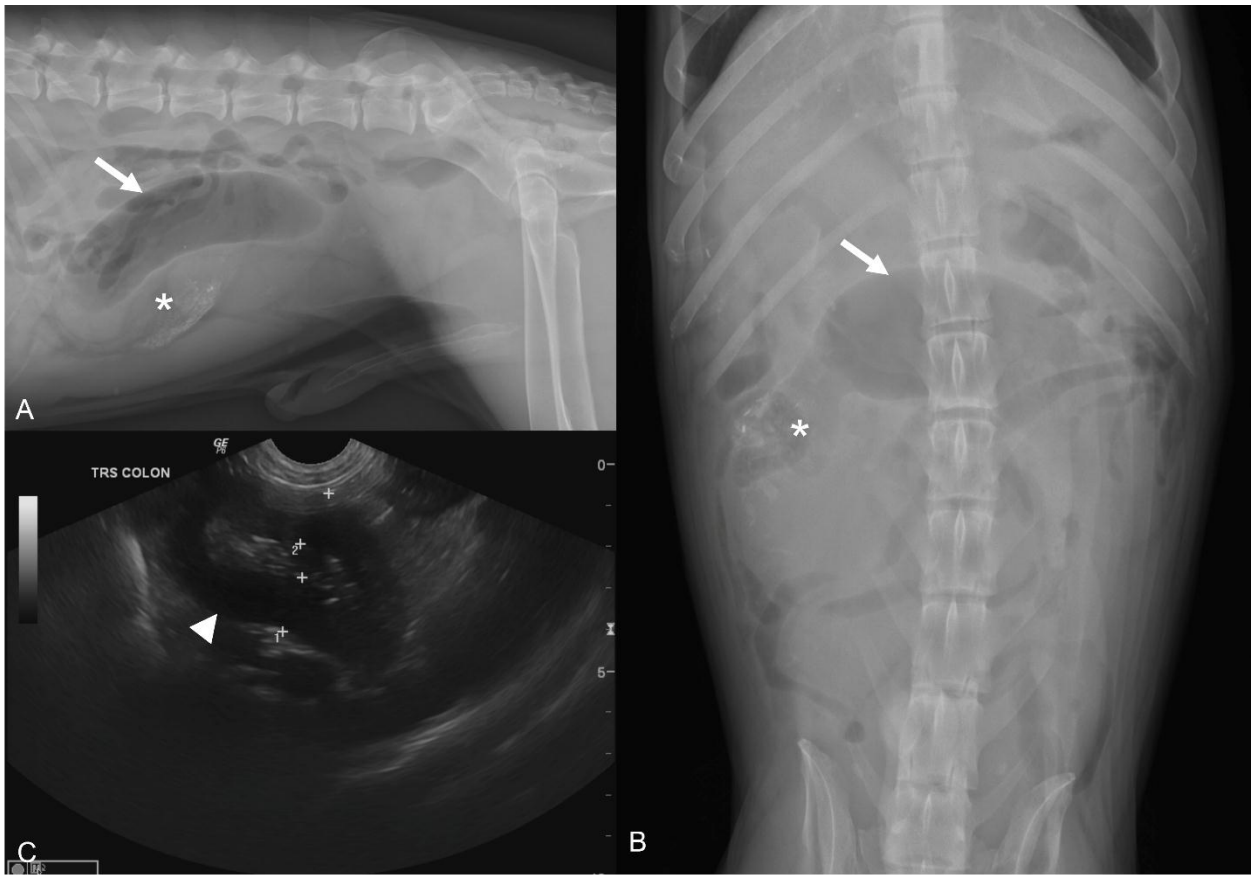

Figure 1 The right lateral (A) and ventrodorsal (B) abdominal radiographs showed focal intestinal ileus (arrow) with multiple small pieces of radiopaque foreign body (asterisk) indicating chronic partial obstruction of the small bowel intestinal loops and the transabdominal ultrasound (C) revealed intramural thickening with loss of wall layering at the transverse colon (arrow head).

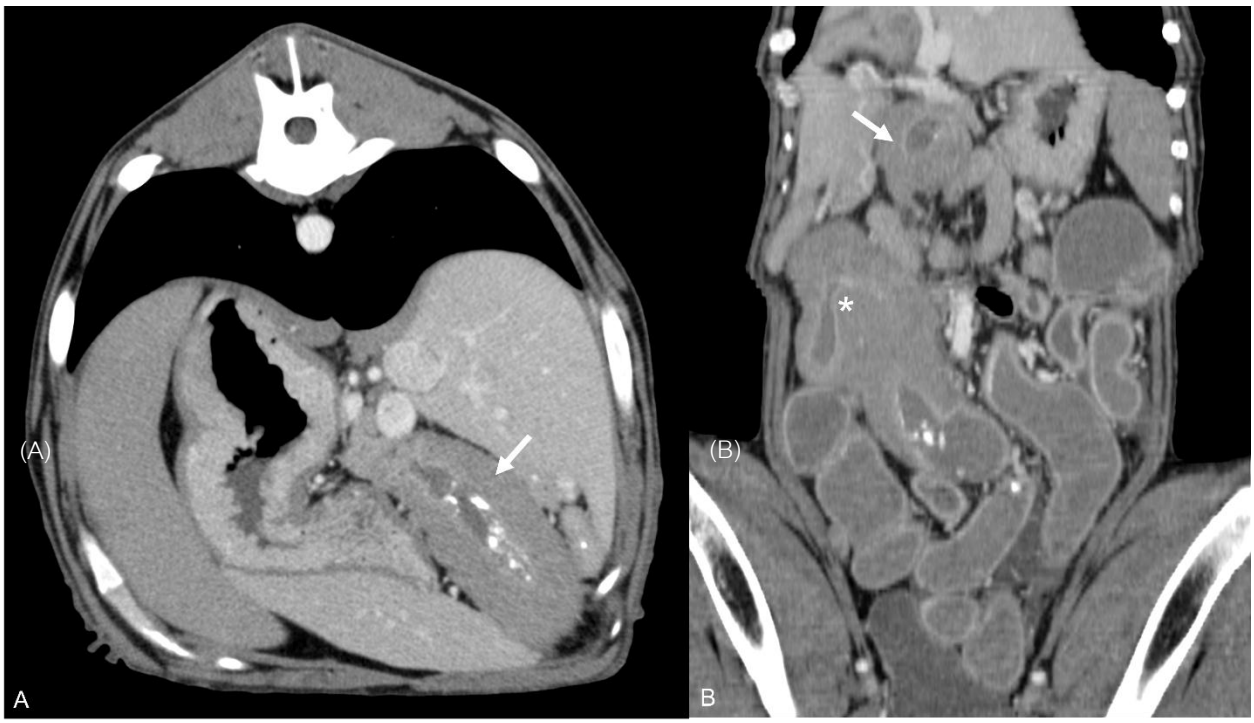

Figure 2 Transverse (A) and dorsal planes (B) of abdominal, contrast enhanced computed tomographic images showed conspicuous circumferential wall thickening of the ascending colon with homogeneous soft tissue attenuation (arrow) and luminal narrowing (asterisk).

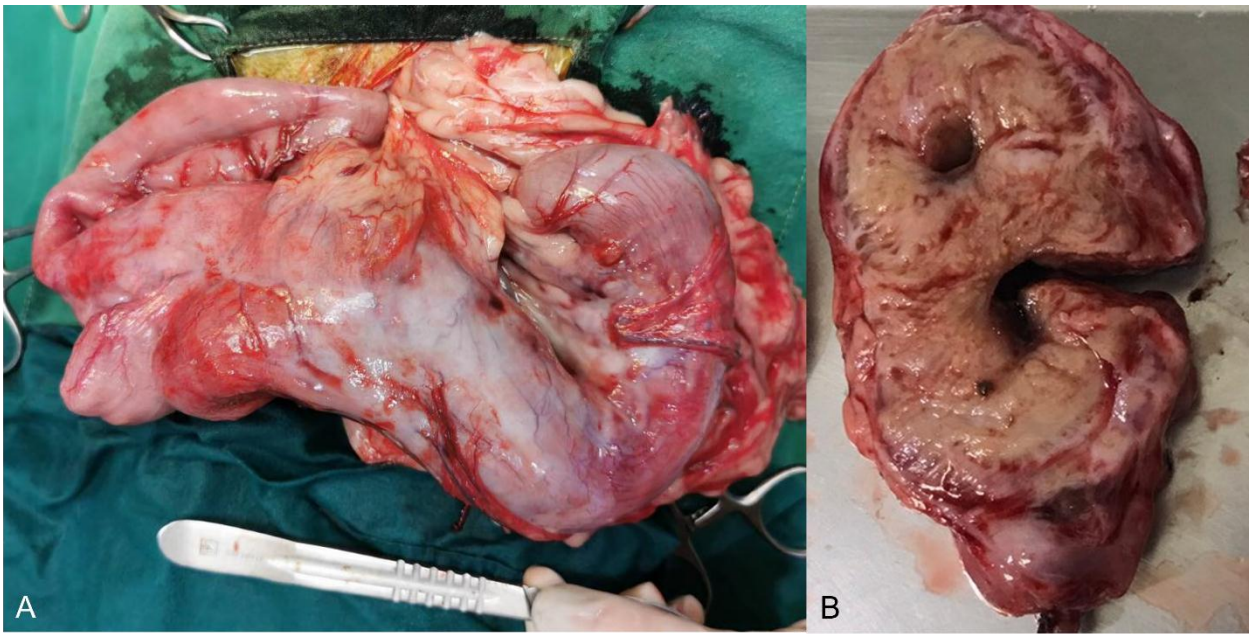

Figure 3 Gross lesion of the affected colon (A) and its cross section (B) revealed granulomatous enteritis with loss of bowel layering.

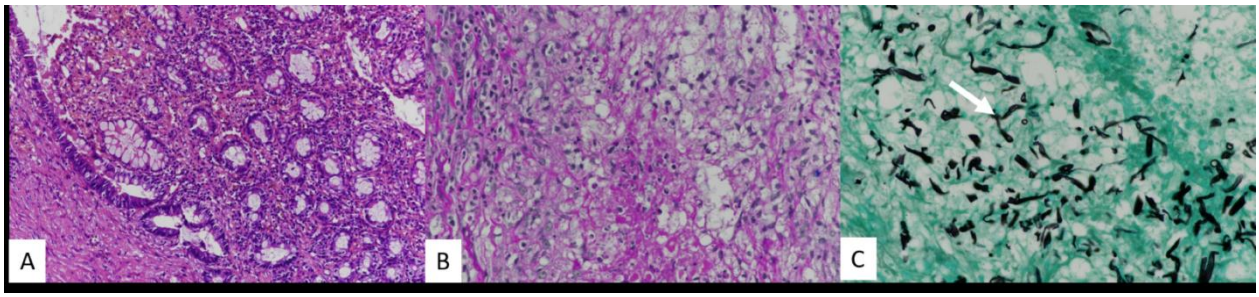

Figure 4 The hematoxylin and eosin (A), Periodic acid-Schiff (PAS; B) and Gomori's methenamine silver (GMS; C) staining of the cross sections of intestinal mass revealed mild hyperplasia of mucosal epithelium and increased chronic granulation tissue to muscular layer. Severe multifocal to coalescing pyogranuloma invaded from serosal to muscular layer and submucosa on dense fibrous stoma. Each pyogranuloma consisted of necrosis, accumulation of segmented neutrophils, macrophages, lymphocyte and plasma cells and mixed with loosely interlacing bundles of collagen fibers and reactive fibroblasts including the positive straining of PAS (bright pink in color) and GMS (brown-black color) indicated intralesional septate branching hyphae of fungal element (arrow).

Discussion

Granulomatous enteritis usually develops due to foreign material or due to infectious pathogens that are cannot be eliminated (Mott and Morrison, 2019). Immunocompromised dogs may be more susceptible to facultative pathogens for example fungal infections resulting in granulomatous enteritis (Seyedmousavi *et al*., 2018). In humans, fungal granulomatous enteritis mostly affects immunocompromised patients via the ingestion of food contaminated with infected soil or animal feces (bats, reptiles, or fish) (Geramizadeh *et al*., 2015) and the most infection sites are colon and rectum followed by the small bowel, liver/gallbladder and stomach (Albaradi *et al*., 2014). The most common gastrointestinal mycosis in humans are *Candida* and *Aspergillus* species (Lamps *et al*., 2014) other fungi such as Basidiobolomycosis (Geramizadeh *et al*., 2015), Histoplamosis (Bhagwat *et al*., 2009; Chávez-Peón Berle *et al*., 2021), Cryptococcosis (Chavapradit and Angkasekwinai, 2018) also have been reported. In dogs and cats, the most common systemic fungal disease are Pythiosis (Berryessa *et al*., 2008; Fortin *et al*., 2017), Aspergillosis (Schultz *et al*., 2008; Ballber *et al*., 2018), Blastomycosis, Histoplasmosis, Coccidiomycosis and Cryptococcosis (Kerl, 2003). Pythiosis is a chronic pyogranulomatous infection of the gastrointestinal tract or skin that is caused by *Pythium insidiosum* (Graham *et al*., 2000). Infection mainly occurs in dogs, horses and humans but rarely in cats (Gaastra *et al*., 2010). *Pythium insidiosum* is a water born pathogen that is commonly found in tropical and subtropical climates; however, infections in animals from temperate areas have also been reported (Berryessa *et al*., 2008). Aspergillosis is a sporadic mycosis, commonly found in soil that occurs in mammals and birds causing disease that mainly affects the nasal cavity and sinuses. The most common forms of aspergillosis in dogs and cats are sinonasal infections (Seyedmousavi *et al*., 2015). Aspergillosis is rare in cats compared with dogs but is considered a severely invasive infection (Hartmann *et al*., 2013). The clinical signs of granulomatous enteritis both in humans and in dogs are similar to other chronic gastrointestinal diseases for example chronic diarrhea, hematochezia, abdominal pain, anorexia, weight loss and lethargy (Chávez-Peón Berle *et al*., 2021). An initial diagnosis of granulomatous enteritis is based on signalment,

history, clinical signs and physical examination, complete blood count and serum biochemistry profiles. Moreover, abdominal radiographs may reveal mass lesions, foreign bodies, signs of obstruction but lower accuracy than ultrasound (Elser *et al.*, 2020). Abdominal ultrasonography can be used to assess entire abdominal organs, examine the whole intestinal tract and to measure wall thickness of intestine. Besides, ultrasound can be used for localization of the disease. In addition, CT scan can clearly provide information for precise assessment of the size and location of the lesion. Moreover, CT scan can assist the surgical planning procedure. Although hematology and serum biochemistry in this case indicated chronic infection or malabsorption it did not show specific abnormalities, histopathology was the diagnostic method to confirm this abnormality. Special staining such as PAS and GMS dye are commonly used to detect fungal spp (Guarner and Brandt, 2011). In addition to histopathology, fungal culture can confirm the specific pathogen causing the disease and fungal culture also allowing for drug sensitivity testing. However, the limitation of fungal culture takes several days to get a result leading to a delay treatment (Kozel and Wickes, 2014). Sometimes, fungal culture is only positive at a late stage of infection (Ellepola and Morrison, 2005). Sensitivity for diagnosis of fungal infection varies with the source and quality of specimen and the skills and experience of laboratorian (Kozel and Wickes, 2014). The treatment of choice for mycotic pyogranulomatous enteritis with good prognosis is complete surgical excision with a combination of antifungal drugs for about two months after resolution of the clinical signs and a minimum of 4-6 month (Mott and Morrison, 2019). Antifungal agents for the treatment of systemic fungal infections in dogs and cats include amphotericin B, fluconazole, itraconazole (Foy and Trepanier, 2010) and terbinafine (Schmiedt *et al.*, 2012). Recurrence after treatment is rare. However, due to the no outcome of fungal culture and good recovery of the dogs without any further intestinal lesions, the client refused post-operative antifungal drug due to the concern about antifungal side effect. Despite no antifungal administration, the dog was well recovered without any recurrent enteritis or intraabdominal lymphadenopathy at up to 5 months post-operatively. Therefore, it might be assumed that completed surgical resection of the infected bowel had been done. In conclusion, in the case of intestinal obstruction by mural lesion, completed investigation including imaging diagnosis of radiography, ultrasonography and CT scan including pre-operative laboratory data proved valuable for treatment guidelines. Besides, in the case of granulomatous enteritis, complete surgical resection and anastomosis would provide the good outcome of the canine patient.

Conflict of interests: The authors declare there are no conflicts of interest.

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