Feline Inflammatory Bowel Disease:

Into the Belly of the Beast

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Introduction

Feline Inflammatory Bowel Disease (IBD) rivals only small cell alimentary lymphoma in prevalence of chronic enteric diseases in cats, especially those middle-aged and older. The majority of cases are between the ages of 8 and 16, and the average age of affected cats is 11 years old [9]. Cats suffering from IBD can be successfully managed for years. Inflammatory episodes can be treated by a simple diet change, routine checks for enteric parasites, or immunosuppressive medications. Many cats have a good quality of life using one or a combination of these treatment modalities [11].

The two most challenging aspects of feline IBD include the non-specific clinical signs and the diagnosis of exclusion. The most common clinical sign of feline IBD is vomiting [1]. Vomiting is not normal for any species, even cats. According to two extensive studies performed at the Alamo Feline Health Center in San Antonio, TX, cats that vomit more than twice in a four week time period have a high probability of suffering from a chronic small bowel disease [9]. IBD and alimentary lymphoma are the two most common chronic small bowel diseases of cats. In the most recent study, 98% of cats that were diagnosed with chronic small bowel disease were confirmed to have either IBD or lymphoma [10].

The critical link between vomiting and IBD is that the associated chronic vomiting likely originates from the small bowel [11]. The duodenum becomes severely inflamed, increasing the amount of stagnant ingesta in the stomach, and vomiting commences [5]. Often, owners will dismiss chronic vomiting at home and fail to report the sign to their veterinarians. Proactively asking all cat owners about vomiting may be a helpful approach to uncovering chronic small bowel diseases, particularly IBD [11]. A cat vomiting more than twice per month is considered abnormal, and indicates an abdominal ultrasound [10].

Measurements of the wall thickness of the small intestines during an abdominal ultrasound have proven to be one of the most helpful tools available for diagnosing small bowel diseases, including IBD [2]. Normal intestinal thickness of healthy cats measures between 0.22cm – 0.30cm [3]. Cats suffering from IBD typically measure greater than 0.3cm in affected segments of the bowel [2]. However, not all cats with IBD have thickened walls of the small intestine [10]. Classically, a cat with the proper clinical signs along with thickened small intestinal walls has an extremely high chance of having one of the two most common chronic diseases of the small bowel [11].

Case Study:

History and Presentation

Coco Sepulveda is a 13 year old male neutered black domestic short hair who presented to Alamo Feline Health Center, San Antonio, TX, on May 23, 2016, for vomiting, weight loss and decreased appetite. Coco's relevant medical history showed that on 6/2/15, an enlarged thyroid gland was palpated, and his free T4 level was 13.9 nmol/L (normal: 0.6 – 1.4 nmol/L). Coco was diagnosed with hyperthyroidism and received I131 treatment on 7/20/16. His thyroid levels returned to normal within 4 weeks, and remained normal at his thyroid recheck on 5/11/16; free T4 was 1.37 nmol/L.

Upon presentation on 5/23/16, Coco's mentation was dull but responsive. He had an unkempt hair coat and body condition score of 3/9. He weighed 4.4 kg. The referring veterinarian had given fluids 3 days prior to presentation to correct his dehydration. Coco was still adequately hydrated. On examination of his abdomen, a firm, thickened area of intestine was palpable and suspicious for a mass. A full diagnostic workup was recommended to the owner, who agreed.

CBC revealed no significant findings; serum chemistry revealed a mild azotemia (Creatinine 2.3 mg/dl, reference range 0.4 – 2.0 mg/dl, and BUN 46 mg/dl, reference range 10-40 mg/dl), and urinalysis revealed isosthenuria with a specific gravity of 1.012.

Abdominal ultrasound revealed that the gallbladder was enlarged, but the liver, stomach, spleen and bladder were normal. The left kidney measured 4.6cm, and the right measured 4.63cm (symmetrical). Small intestinal wall thicknesses ranged from 0.20-0.45cm. The area which measured 0.45cm was suspicious of a soft tissue mass. Due to the amount of evidence suggesting a chronic small bowel disease, an exploratory laparotomy was recommended.

Coco was admitted in-hospital and given an injection of enrofloxacin at 5.2mg/kg . LRS fluids were given intravenously at maintenance rate and ran overnight.

On the morning of 5/24/16, Coco underwent pre-operative screening. His physical exam and EKG were normal. Coco was given subcutaneous injections of buprenorphine at 0.1mg/kg, Acepromazine at 0.05mg/kg, a second dose of enrofloxacin at 5.2mg/kg and cefovecin. He was induced and maintained on 1.4% isoflurane.

Coco was placed in dorsal recumbency, and his abdomen was sterilely prepped. An approximately 5cm skin incision was made, his abdominal body wall was opened, and his intestines were exposed. The entire small bowel was examined from the duodenum to the most caudal portion of the ileum. The cecum and proximal half of the large bowel were also inspected. The jejunum was hyperemic and edematous in multiple segments, and one section had a thickened area suspicious of a mass. Three 6mm full-thickness punch biopsies were taken at areas of inflammation. A 6mm full-thickness punch biopsy was also taken of the duodenum and ileum. A 6cm section of jejunum, including the thickened area suspicious of the mass, was

removed by resection and anastomosis. During the laparotomy, additional wedge biopsies were taken of the pancreas and liver to check for concurrent inflammatory or neoplastic diseases. The stomach and large colon were both checked for inflammation and/or thickening, but both were normal. Coco's abdomen was closed routinely in three layers.

While Coco was under anesthesia, an esophageal feeding tube was placed in the left side of his neck. The feeding tube was placed due to Coco's recent anorexia and high risk of hepatic lipidosis. Coco recovered uneventfully from anesthesia and spent the next 4 nights in-hospital for observation and pain control.

On 5/26/16, enrofloxacin and fluids were continued. Post-operative blood work revealed the pre-operative azotemia had resolved (Creatinine 1.4mg/dL, BUN 21mg/dL). However, Coco's phosphorus was decreased at 2.6mg/dL (normal range: 3.4 – 6mg/dL), and his hematocrit was 20% (normal range: 30-45%). Darbepoetin at 1.4mcg/kg was started to address the anemia, and calcitriol at 8.7ng/kg was started to increase Coco's calcium levels. The latter was prescribed with the intent of long-term therapy.

On 5/27/16, Coco was taken off fluids, and all medications were given through the esophageal tube. On 5/28/16, Coco was sent home, and the owners were instructed how to feed Coco through the esophageal tube. Biopsy results of the liver sample indicated mild, diffuse hepatic lipidosis, so Coco's esophageal tube stayed in place for 2 weeks. Coco returned on 6/3/16 for a recheck examination and suture removal. The owner reported that Coco was doing well at home.

The biopsies of Coco's small intestines revealed fibrosing enteropathy along with lymphoplasmacytic and eosinophilic enteritis. The enteritis was diffuse and severe with focally extensive ulceration, transmural inflammation, fibroblasts and multifocal fibrinoid vasculitis.

The biopsy of the pancreas showed moderately diffuse atrophy.

The histopathology report stated:

"The mass lesion in the small intestine is a focally extensive area of ulceration with transmural inflammation. Much of the small intestines have very blunted villi with abundant fibrosis and loss of crypts. The intestine is diffusely atrophied and fibrotic suggesting that there was previous severe enteritis that has left the intestine with minimal regenerative capacity. The eosinophils are most likely due to defective mucosa allowing foreign protein to leak into the mucosa. There is no evidence of neoplasia."

Pathophysiology:

During an episode of intestinal upset due to IBD, the pathophysiology involves increased permeability of the Gut-Associated Lymphoid Tissue (GALT) [8]. Normally, a layer of mucus called the Intestinal Mucosal Barrier (IMB) coats the GALT and prevents access by antigens. If food allergens or antigens breach the IMB and reach the GALT, an immune response is triggered. Any breach made by enteric flora or non-allergen food material will not trigger a GALT immune response in normal, healthy intestinal tissue [5].

Chronic enteritis occurs when the GALT responds inappropriately to enteric flora, non-allergen food, or responds excessively to pathogens and allergens [5]. Specifically, T-cells respond to enteric flora inappropriately, aggressively, and segmentally. Lymphoplasmacytic cells respond as an influx within the normal intestinal tissue, causing inflammation [8]. The duodenum is the most commonly affected area. The muscularis propria becomes thickened, which can be visible on ultrasound. The normal intestinal wall measures <0.28cm. A thickened muscularis propria causes the overall wall thickness to increase, and IBD typically presents with a wall thickness of >0.30cm [2]. The disease ultimately manifests with non-specific clinical signs, such as

abdominal pain, decreased appetite, vomiting, weight loss, and occasionally, palpably thickened intestinal segments [11].

Diagnostic Approach

Diagnosis of IBD starts with a thorough history from the owner. Non-specific clinical signs, such as vomiting, diarrhea, and weight loss, are the typical presenting problems [1]. Owners historically overlook or dismiss such clinical signs, especially vomiting, and may consider them as normal for the cat. If the owner of the cat considers vomiting to be normal, s/he may mentally dismiss this important clue. Veterinarians must proactively ask about chronic vomiting, intermittent diarrhea, and weight loss during each exam, especially wellness exams. According to one study, 25% of cats diagnosed with chronic small bowel disease were found during routine checkups [9].

According to the study, 100 cats diagnosed with chronic small bowel disease underwent exploratory laparotomies to obtain full-thickness biopsies of the duodenum, ileum, and any areas of suspected inflammation. The histopathological reports of the biopsies revealed that of the 100 cats, 49 were diagnosed with lymphoplasmacytic enteritis. Fifty cats were diagnosed with intestinal neoplasia, including small cell lymphoma, and 1 cat showed no significant findings on histology [9].

IBD is the most common non-cancerous enteric disease of cats. The trademark histopathological feature is lymphoplasmacytic inflammation, especially in the muscularis propria layer of the small intestinal wall [5]. The most common locations to find the lymphoplasmacytic inflammation are the duodenum followed by the ileum. Full-thickness biopsies of the duodenum, ileum, and any areas of suspected inflammation, advanced diagnostic imaging,

including abdominal ultrasound, and a thorough analysis of clinical signs provide the most useful data when diagnosing a suspecting case of IBD [9].

Considerations

Feline IBD is especially difficult to diagnose due to the vast similarities with alimentary lymphoma. Each disease affects the small intestines of cats, most of which are middle-aged to older [5]. Clinical signs are non-specific for lymphoma, including decreased appetite, diarrhea, and weight loss [2]. Intermittent vomiting occurs in both diseases frequently, but IBD has been linked to more cases than lymphoma. On cytology, both diseases can cause a leukocytosis, hypoproteinemia as well as an increase in hepatic enzymes [1].

Advanced imaging has played a key role in diagnosing feline chronic small bowel diseases; however, IBD and lymphoma cannot be differentiated solely by imaging. On abdominal ultrasound, both diseases show a thickening of the muscularis propria layer of the small intestinal wall [2]. On endoscopy, both IBD and lymphoma can appear as a friable, thickened mucosa with lymphoid hyperplasia [7].

Endoscopy can be useful in diagnosing feline chronic small bowel diseases, as well. Not all cats are good candidates for surgery, and esophagogastro-duodenoscopy (EGD) is much less invasive than laparotomy, in which dehiscence is a possibility [7]. Mucosal biopsies can be taken quickly, but endoscopic biopsies are limited in diagnostic value because samples of the muscularis propria are generally not achievable [10].

Diagnosing IBD from lymphoma is not always possible, due to a variety of reasons, such as financial constraints of the owner or high anesthetic risk of the cat. In the event that circumstances favor an accurate diagnosis, the prognosis of the cat could be the deciding factor

on to treat or not to treat [5]. When diagnosed early in the disease, IBD has a good to excellent prognosis. An uncomplicated case of IBD, without concurrent diseases such as triaditis, can be successfully managed for years [2]. Involvement of the liver and pancreas, such as hepatic lipidosis and pancreatitis, along with an inflamed bowel (triaditis) downgrades the prognosis, but the cat still has a favorable chance for a high quality of life [5].

Furthermore, IBD and lymphoma can occur concurrently. As IBD progresses and the disease process worsens, there is an increased risk for the development of alimentary T-cell lymphoma. Chronic cases of untreated IBD have led to lymphoma, which result in increased morbidity [5].

Treatment & Management Options

The approach to the treatment of IBD needs to be tailored to the individual cat, taking into consideration the severity of the disease, concurrent problems, and financial capabilities of the owner, among other variables. Milder cases may only need a change in diet, while more severe cases may require immunosuppressive therapy, including chemo therapy [5], [11].

With Coco's confirmed diagnosis of IBD, the recommended protocol of diet change, maropitant, and immunosuppressant medications was presented to the owner. Coco's diet was not changed to a novel protein cat food due to external factors, but he did well with the esophageal tube. After the tube was removed, he switched to a dry kibble and a probiotic was added. The vomiting was well controlled with oral maropitant at 2mg/kg once per day for five days. The financial limitations and lack of compliance of the owner prevented Coco from starting the immunosuppressant medications.

According to one author's opinion, an immunosuppressant regimen should begin the day the sutures are removed from the incision site, which is around day 14. On this day, an injection of

Depo-Medrol at 20mg, an oral dose of lomustine based on body weight, and an injection of B12 vitamin are administered. This regimen, along with a CBC, is continued every 4 weeks for a total of 6 treatments. On the 6th visit, an abdominal ultrasound is performed to measure the wall thickness of the small intestines [11].

Corticosteroids have been used alone or concurrently with other immunosuppressive drugs and have been successful at controlling clinical signs of IBD [5]. Cyclosporine and chemotherapy agents have been beneficial in conjunction with corticosteroids [10]. Chlorambucil, as well as lomustine, are well-tolerated in cats and work well as immunosuppressive agents. Cats with IBD can be managed for years with immunosuppressive drugs and still maintain a good quality of life [5].

Not all IBD cases can have a definitive diagnosis, and treating for multiple gastrointestinal diseases can help improve the cat's condition without significant financial burden on the owner [11]. A successful protocol used by Dr. Gary Norsworthy begins on day 1 by starting a food trial of a novel protein diet to rule out any food allergies. At the same time, start twice weekly injections of B12 at 100mcg per dose. Continue the food trial and B12 for at least 6 weeks. Also on day 1, start fenbendazole at 100mg orally every 24 hours for 5 days to rule out gastrointestinal parasites, such as *Giardia* or *Physaloptera*. Once the fenbendazole has been completed, start metronidazole at 15-25mg/kg orally once per day for 5 weeks, and add a probiotic to the diet [12].

Nutritional support is paramount for treating IBD [5]. Enterocytes heal faster with proper nutrition [7]. Vomiting, diarrhea, and decreased appetite are common clinical signs associated with IBD, and each has the capability of preventing the proper absorption of nutrients from the GI tract [1]. Providing a short-term esophageal tube speeds up the recovery of episodic bouts of

IBD, and percutaneous endoscopic gastrostomy (PEG) tubes provide long-term supportive care [7].

Case Outcome

Coco did well post-operatively. At his 2 month recheck, he had gained 0.4 pounds, and his vomiting had resolved. Blood work revealed that his creatinine had decreased and was within normal limits. Physical exam was normal, and the owner stated that he was doing very well at home. At the 6 month recheck, Coco's appetite had decreased; however, the owner was no longer feeding him the recommended diet. According to the owner, he had recently become PU/PD. As of February 13, 2017, Coco had no problems regarding his IBD and primarily visits his regular veterinarian for rechecks of his kidney disease.

References:

[1] Batchelor, Daniel J. Devauchelle P. Elliot J. et al. Mechanisms, causes, investigation and management of vomiting disorders in cats: a literature review. *Journal of Feline Medicine and Surgery 2013;* 15(4): 237-265.

[2] Daniaux, Lise A. Laurenson M. Marks S. et al. Ultrasonographic thickening of the muscularis propria in feline small intestinal small cell T-cell lymphoma and inflammatory bowel disease. *Journal of Feline Medicine and Surgery 2014;* 16(2):89-98.

[3] Donato, Pameli D. Penninck D. Pietra M. et al. Ultrasonographic measurement of the relative thickness of intestinal wall layers in clinically healthy cats. *Journal of Feline Medicine and Surgery 2014;* 16(4): 333-339.

[4] Hahn, Harriet, Pey, P. Baril A. et al. Ultrasonographic, endoscopic and histological appearances of the caecum in cats presenting with chronic clinical signs of caecocolic disease. *Journal of Feline Medicine and Surgery 2017;* 19(2) 94-104.

[5] Jergens, Albert E. Feline Idiopathic Inflammatory Bowel Disease: What we know and what remains to be unraveled. *Journal of Feline Medicine and Surgery 2012;* 14: 445-458.

[6] Maunder, Christina L. Day M. Hibbert A. et al. Serum cobalamin concentrations in cats with gastrointestinal signs: correlation with histopathological findings and duration of clinical signs. *Journal of Feline Medicine and Surgery 2013;* 14(10): 686-693.

[7] Neiger, Reto. Robertson, E. Stengel C. Gastrointestinal Endoscopy in the Cat: Diagnostics and therapeutics. *Journal of Feline Medicine and Surgery 2013;* 15: 993-1005.

[8] Nelson, Richard L. & Couto C. G. *Small Animal Internal Medicine*. 4th Ed. Elsevier Health Sciences. 2008.

[9] Norsworthy, G.D. Scot Estep J. Kiupel M. et al. Diagnosis of chronic small bowel disease in cats: 100 cases (2008-2012). *Journal of the American Veterinary Association 2013;* 243(10): 1455-1461.

[10] Norsworthy, G. D. Scot Estep J. Hollinger C et al. Prevalence and underlying causes of histologic abnormalities in cats suspected to have chronic small bowel disease: 300 cases (2008-2013). *Journal of the American Veterinary Association 2015;* 247(6): 629-635.

[11] Norsworthy, G. D. Chronic Small Bowel Disease in Cats. *Advances in Small Animal Medicine and Surgery 2016;* 29(1): 1-3.

[12] Norsworthy, G.D. Chronic Vomiting: Should We Ask a Cat to Live with It? *Vetcom 2014;* Vol. 53: 10-14.

[13] Tucker, Samuel. Penninck D. Keating J. et al. Clinicopathological and ultrasonographic features of cats with eosinophilic enteritis. *Journal of Feline Medicine and Surgery 2014;* 16(12): 950-956.