[Case Report #]

Signalment

10 year old, Spayed Female, Domestic Short Hair

Patient History

Misty presented to our facility on June 23, with a 48-hour history of bilious vomiting and 36-hour history of anorexia. The owners were unsure about litter box habits, as there is another cat in the household. The owners reported no known exposure to toxins or any dietary indiscretion. Misty was strictly an indoor cat.

Initial Exam Findings

Upon arrival at AAH, Misty was bright, alert, and responsive. Her physical exam revealed: weight 6.68 lbs / 3.04 kg, body condition score 5/9, HR 180 bpm, slight tachypnea (RR 48), and normothermia (102.0°F). She was estimated to be approximately 5% dehydrated, with light pink mucous membranes (MM) and a capillary refill time (CRT) of <2s. Her thorax ausculted with evidence of a murmur and without adventitious lung sounds. Her abdomen was tense and painful on palpation. The Applicant collected appropriate samples for CBC, serum chemistries, fPLi (via SNAP® test), and electrolytes. The results were as follows: leukocytosis ($22.3x10^3/\mu l$, N=5-19.5 $x10^3/\mu l$); ALT 625U/L (N=20-100U/L); total bilirubin (t.bili) 2.7mg/dl (N=0.1-0.6mg/dl); potassium 3.3mEq/L (N=3.7-5.8mEq/L); and an abnormal fPLi SNAP® result.

Problem List

Misty's problem list included: leukocytosis, elevated ALT and t.bili, hypokalemia, and an abnormal fPLi. Her prognosis was fair to good pending response to treatment.

Veterinarian's Differential Diagnosis

Misty's differential diagnosis list included: pancreatitis, hepatic lipidosis, triaditis, cholangiohepatitis, inflammatory bowel disease, neoplasia (lymphoma).

Initial Diagnostics and Interventions

Misty was admitted to the AAH ICU for supportive care and further diagnostics including abdominal ultrasound (AUS), urinalysis with culture, PT/aPTT, Feline Specific PLi (Spec fPLi), thyroid testing, and repeated measurements of electrolyte, CBCs, and liver enzymes. The Applicant assisted the DVM with the AUS and found: dilated bile ducts with hyperechoic hepatic parenchyma, mesenteric lymphadenopathy, slightly thickened small intestinal walls, and debris in the urinary bladder. The pancreas itself was ultrasonographically normal, as was the gall bladder. The Applicant performed a clean cystocentesis to obtain a sterile urine sample for in-house urinalysis and urine culture to be sent to an outside lab. The Applicant performed the urinalysis and found: urine specific gravity >1.050 (N=1.018-1.050); proteinuria; glucosuria; and bilirubinuria. Review of a stained slide revealed bilirubin crystaluria with no evidence of pyuria or bacteriuria. A urine sample was sent to the lab for culture. Spec fPLi result was 44.7ug/L (N=0-3.5ug/L) indicating pancreatitis and T4 was 1.7µg/dl (N= 0.8-4.0µg/dl) indicating normal thyroid function. With the new information from the ultrasound, a working diagnosis of inflamed small intestines (presumed inflammatory bowel disease), cholangiohepatitis and pancreatitis

(also known as triaditis) was made. The Applicant placed a 20g IV catheter into the right cephalic vein and initiated balanced crystalloid IV fluid therapy at 15ml/hr. Misty was maintained on a KCl CRI of 20mEq/L of fluids. The Applicant calculated and administered: buprenorphine 0.02mg/kg (0.1ml) transmucosally TID per the DVM's orders to treat Misty's abdominal pain. To treat Misty's nausea from pancreatitis, the Applicant calculated and administered the following medications per the DVM's orders: maropitant 1mg/kg (3mg) IV SID; ondansetron 1mg/kg (3mg) IV SID; pantoprazole 0.7mg/kg (2.12mg) IV SID to reduce acid production; sucralfate 164mg/kg (500mg) PO TID for stomach lining protection and repair. To address the liver inflammation, the Applicant calculated and administered ursodiol 15mg/kg (46mg) PO SID per the DVM's orders. To treat the presumed ascending infection from the small intestines to the liver, the DVM ordered and the Applicant calculated ampicillin 22mg/kg (67mg) IV TID; metronidazole 10mg/kg (30mg) IV BID. As the bacterial growth decreases, so does the amount of toxins the liver must filter. The DVM also ordered mirtazapine 1.2mg/kg (3.75mg) PO q72h to stimulate Misty's appetite, which was calculated and administered by the Applicant.

Eight hours after Misty was admitted to the ICU, the DVM ordered placement of a nasogastric (NG) tube. This would allow the ICU staff to provide enteral nutrition, as it had been close to 48-hours since Misty had eaten. The Applicant confirmed that Misty was able to clot appropriately (PT 15.9s [N=15-21s]; aPTT 113.2s [N=86-137s]) prior to administering butorphanol 0.33mg/kg 1mg (0.1ml) IV and midazolam 0.16mg/kg 0.5mg (0.1ml) IV one time to facilitate NG tube placement (per the DVM's orders). The Applicant placed the NG tube and verified proper placement via thoracic radiography with DVM confirmation. Daily caloric

requirements were calculated using the formula: 70 x ($BW_{kg}^{0.75}$) and determined to be 160kcal/ day. The Applicant used liquid nutrition with a concentration of 1kcal/ml (Clinicare®) for the tube feeding. Per the DVM's orders, the Applicant initiated trickle feeding at 25% RER over the first 24 hours (60kcal/ day, 1.7ml/hr). The feeding plan was to increase the trickle feeding by 25% RER every 24 hours until 100% RER was achieved. The rate increase was dependent on how well Misty tolerated her feeding as evidenced by lack of signs of nausea such as vomiting or regurgitation. Forty-eight hours after initiating trickle feeding, Misty began to improve and to eat ravenously on her own. At this time, all injectable medications were discontinued and the following oral medications were initiated: amoxicillin 33.3mg/kg (100mg) PO BID; omeprazole 0.7mg/kg (2.2mg) PO SID; and metronidazole 15.3mg/kg (46mg) PO BID. The previously prescribed oral medications (buprenorphine and ursodiol) were continued. Serum chemistries and electrolytes were rechecked at this time, and the results were as follows: improved ALT 250U/L; improved t.bili 0.89mg/dl; and improved potassium 3.9mEqL. The KCl CRI was discontinued due to updated potassium results. On June 27, since Misty was eating well on her own, tolerating her oral medications and had improvements in her chemistry values, the DVM decided to remove her NG tube and discharge Misty to her owners. In addition to the oral medications Misty was discharged with (as previously prescribed and administered in-hospital), the DVM recommended her diet be changed to a hypoallergenic formula to treat the presumed inflammatory bowel disease. The Applicant prepared both the dry kibble version and canned version of the hypoallergenic diet for the owners. The Applicant relayed the DVM's orders to have Misty rechecked 5 days after discharge for recheck evaluation and blood work.

Outcome

Misty returned on July 3 for recheck evaluation and blood work. She continued to eat the hypoallergenic diet well on her own, but it was becoming difficult with for her owners to administer oral medications. The blood results were as follows: t.bili 0.24mg/dl; ALT 86U/L; and Spec fPLi 1.2µg/dl. The Applicant relayed the DVM's orders to Misty's owners to discontinue all oral medications and to recheck in one month for evaluation and blood work.

Unfortunately, Misty has neither returned for her recheck evaluation, nor presented for humane euthanasia. Therefore she is presumed to be doing well without medications at this time.

Discussion of Case

Misty was suffering from pancreatitis, cholangiohepatitis, and presumed inflammatory bowel disease. When these three disease components are present, the syndrome is referred to as triaditis.

Pancreatitis is a condition where an excess of the digestive enzyme trypsin auto-activates in the pancreas. This excess overwhelms the protective mechanisms and a chain reaction begins: trypsin activates more trypsin, amylase, and lipase excretion in the pancreas leading to auto-digestion, inflammation and peripancreatic fat necrosis[1]. Cats that develop pancreatitis are at a higher risk of developing hepatic lipidosis[2] due to rapid weight loss and anorexia, and therefore every effort should be made to institute enteral feeding within 48 hours[3]. Hepatic lipidosis is a potentially life threatening complication of pancreatitis wherein the patient develops an acute hepatopathy where a large volume of fat accumulates in the hepatocytes leading to loss of

hepatic function. Loss of hepatocyte function is due to the distention of the triglyceride vacuoles within the hepatocyte causing canalicular compression,[4] which does not allow the hepatocyte to function properly. The hepatocyte function is to synthesize bile and to secrete the bile into the biliary ducts via the canalicus. Treatment for pancreatitis is aimed at controlling the symptoms, such as anorexia and vomiting, and managing the patient's pain appropriately Patients suffering from pancreatitis can become dehydrated from vomiting and anorexia; therefore IV fluids are helpful in maintaining appropriate hydration status. A common complication of pancreatitis is systemic inflammatory response syndrome (SIRS) and increased vascular permeability[5]. Due to this increased vascular permeability, it is important to accurately monitor the patient's ins/outs as well as other parameters like heart rate and respiratory rate. A potential complication of increased vascular permeability is fluid leaking out of the intravascular space and into the interstitial space, which can lead to edema of the extremities, and reduced cardiac output which can results in hypotension. SIRS can lead to other complications such as multiorgan failure (MODS) and diffuse intravascular coagulation (DIC)[6] due to the body's release of cytokines. Monitoring for any changes in the patients status could indicate one or a combination of these complications. As these complications manifest, the patient may suffer from some of, or all, of the following changes during the Applicant's exam: HR >140-160 bpm, T <100F or >103F, and RR >28[7]. The Applicant must also be on guard for ecchymoses, hematechezia or melena, bleeding from venipuncture sites and changes in CBC and blood chemistry values which may indicate DIC.

In some cases of pancreatitis, extrahepatic biliary obstruction may occur due to the inflammation of the pancreas and liver. Signs of an extrahepatic biliary obstruction include: vomiting, anorexia, and jaundice. In general, no invasive action is needed as the obstruction usually resolves with conservative medical management.[8] Prognosis is dependent on the severity of the pancreatitis ranging from grave to good.

Inflammatory bowel disease (IBD) is believed to be due to an inappropriate response by the intestinal immune system to bacterial and/or dietary antigens[9]. Symptoms of IBD include vomiting, small bowel diarrhea, and weight loss. Small bowel diarrhea is characterized by its large volume, with only a slight increase in frequency, if any. In severe cases, protein-losing enteropathy can occur due to the increased permeability of the intestinal mucosa to proteins. Increased permeability of the gut can be due to mucosal injury or to malabsorption of nutrients from the lumen of the GI tract. A differential diagnosis for these symptoms in the cat is alimentary lymphoma. IBD and alimentary lymphoma closely resemble each other both clinically and histologically.[10] Because of the possibility of lymphoma, an endoscopy or exploratory laparotomy would be warranted to obtain full thickness biopsies of the alimentary tract to help differentiate between lymphoma and other causes of inflammation. The owners were offered these options, but declined due to the perceived risks of general anesthesia. That being said, the owners would have pursued this option if Misty had not improved with empirical treatment. Treatment for IBD usually starts with eliminating dietary allergens such as beef, fish, and chicken. This is achieved by feeding a novel protein diet, which is a diet that consists of a protein source that has not ever been offered to the patient, such as kangaroo. If an elimination

diet does not get eliminate clinical signs, corticosteroids may be necessary[11]. Corticosteroids, such as prednisolone, have potent anti-inflammatory and immunosuppressive properties, which help reduce the inflammation in the gut. Any drug therapy should continue two to four weeks past resolution of symptoms before attempts at weaning medications should be made. This helps to ensure the improvement in symptoms is a true improvement as opposed to an unrelated event. If treatment is begun when the patient still has a normal BCS (4-5/9), prognosis is generally good[12].

Cholangiohepatitis is inflammation of the biliary tract that extends into the hepatic parenchyma and is more common in cats than in dogs.[13]Cholangiohepatitis is divided into three categories depending on its etiology: neutrophilic cholangiohepatitis, lymphocytic cholangiohepatitis, and chronic cholangiohepatitis due to liver fluke infestation. Misty had not traveled to an area where liver flukes are common, nor did she have a long history of low-grade illness (indicative of lymphocytic cholangiohepatitis).[14] Due to Misty's history, the DVM presumed she was suffering from neutrophilic cholangiohepatitis, which is believed to be caused by an ascending bacterial infection originating from the small intestine.[15] The most accurate diagnosis of neutrophilic cholangiohepatitis is from cytology and culture of the bile.[16] To obtain a sample of bile from Misty's gall bladder, heavy sedation or general anesthesia would have been required and – because of the perceived risk of general anesthesia, coupled with the potential risks of the sampling procedure (including gall bladder rupture and bile leakage) – the owners declined. With the DVM's guidance, the owners opted for medical management of presumed neutrophilic cholangiohepatitis. Medical management included amoxicillin and metronidazole as

empirical treatment for a potential intestinal bacterial infection, and ursodiol as an anti-inflammatory agent in the gall bladder. Prognosis for neutrophilic cholangiohepatitis is good, and a full recovery is expected in most cases.

These three diseases - pancreatitis, IBD, and neutrophilic cholangiohepatitis - commonly occur at the same time. Prognosis for IBD and neutrophilic cholangiohepatitis is usually good; therefore, the overall prognosis for triaditis patients is dependent upon the severity of pancreatitis. In Misty's specific case, recommendations included a hypoallergenic diet to both treat her IBD and manage her pancreatitis, along with intermittent antibiotics, as needed to treat bouts of neutrophilic cholangiohepatitis. Even with diligent attention to the recommended treatment regimen, Misty still may require further hospitalization for treatment of triaditis.

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APPENDIX I: Laboratory and Diagnostic Reports

HEMATOLOGY LAB CHART

Test:	Reference	Date: 6/23/15	Date: 6/24/15	Date: 6/25/15	Date: 7/5/15
WBC	5.5-19.5x10^3/µL	22.3	16.7	23	8.65
RBC	5.00-11.00x10^6/µL	7.34	7.15	5.68	6.78
HGB	8.0-15.0g/dl	11.1	10.1	8	9.51
HCT	25.0-45.0%	30.3	28.9	23	27.8
MCV	39.0-50.0fl	41.2	41	40	41
MCHC	31.0-38.5g/dl	36.6	35	36	34.2
PLATELET	200-500x10^3/µL	66	245	361	247
SEGS	60.0-77.0 x10^3/µL		91	93	84
ABSONEUT	3,000-11,500 x10^3/µL		15,200.00	21,400.00	7,266.00
LYMPHS	12.0-30.0%	8.1	5	3	11
ABLYMPH	1,000-4,800 x10^3/µL	1.8	887	690	951.5
MONOS	%	10.2	0	3	1
ABSMONO	150-1350 x10^3/µL	2.3	0	690	86
EOS	2.0-10.0%		2	0	4
ABSEOS	100-1,250 x10^3/µL		1,340.00	0	346
BANDS	0-3.0 %		2	0	0
ABSBANDS	0-300 x10^3/µL		1,340.00	0	0
PT	15-21sec	15.9			
aPTT	86-137sec	113.2			

URINALYSIS

Test	Reference	Date: 6/24/15

COLOR		Dk. Yellow
SPGR	1.015-1.060	1.068
PH	5.5-7.0	7
PRO		3+
GLUC		1+
KETO		Negative
BILI		3+
BLOOD		Negative

CHEMISTRY

Test	Reference	Date: 6/23/15	Date: 6/24/15	Date: 6/25/15	Date: 7/5/15
GLU	70-150mg/dL	173	117.25	108.52	96.7
BUN	10-30mg/dL	13	15.92	21.4	23.42
CREA	0.3-2.1mg/dL	1			
Ca	8.0-11.8mg/dL	9.6			
PHOS	3.4-8.5mg/dL	4.4			
TP	5.4-8.2g/dL	8.2	6.1	5.8	6.9
ALB	2.2-4.4g/dL	3	2.27	2.19	2.38
GLOB	1.5-5.7g/dL	5.2			
ALT	20-100U/L	625	364	250	86
ALKP	5-70U/L	45	65.88	64.35	47.03
GGT	1-10U/L		4.65	1.28	0.9
TBIL	0.01-1mg/dL	2.7	3.291	0.892	0.24
Na+	142-164mmol/L	143			
K+	3.7-5.8mmol/L	3.3	4.5	3.9	4.4
Cl-	112.0-129.0mmol/L	117			
AMY	300-1100U/L	670			
Specific fPL	0-3.5ug/L	44.7			1.2
T4	0.8-4.0µg/dL	1.7			