“Skipper’s Pancreatic Predicament”

Pancreatic Abscess formation after Acute Pancreatitis in a Fox Terrier

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Class of 2020

Clinicopathologic Conference

February 14, 2020

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Introduction

While pancreatitis is a common disease process in the canine patient, its pathophysiology diagnosis, and treatment still raise many questions in veterinary medicine. Acute pancreatitis is a multifactorial process that is thought to be caused by an inappropriate activation of zymogens within the pancreatic parenchyma.[5] This incites an influx of neutrophils into the pancreas and leads to inflammation. As this inflammation worsens, the pancreatic blood flow decreases; this, in combination with the inflammation, leads to necrosis of the pancreatic parenchyma and possible abscessation of the pancreas.[5] There are many different reported causes for pancreatitis with the most common being dietary factors and hyperlipidemia.[8] Clinical signs of acute pancreatitis include, but are not limited to, the sudden onset of anorexia, vomiting, depression, and abdominal discomfort.[8] The gold standard for the diagnosis of acute pancreatitis is histopathology; however, due to the invasive nature of this and the limitations it has, many other diagnostic tools are utilized.[2] These tools include clinicopathological abnormalities, pancreatic ultrasound, and pancreatic lipase concentration.[2] The mainstay of treatment for cases of acute pancreatitis is to combat dehydration with intravenous fluids, control emesis and gastric acid with anti-emetics and proton pump inhibitors, and to control pain with intravenous pain medication.[5] Other more controversial treatments include early nutritional management and the use of corticosteroids.[5] The incidence of acute pancreatitis in small animal veterinary medicine is common, and uncomplicated cases can be adequately treated in most general veterinary practices.

History and Presentation

Skipper is an approximately 5-year-old female spayed Fox Terrier who presented to MSU-CVM Internal Medicine Department on 9/4/2019 for the evaluation of a potential

pancreatic abscess. Skipper had previously been admitted to Animal Emergency and Referral Center (AERC) of Jackson, MS on 8/26/2019 for lethargy and inappetence and was diagnosed with acute pancreatitis. She was treated as an inpatient with 1 mg/kg Cerenia intravenously given daily, 1 mg/kg Pantoprazole intravenously every 12 hours, 0.2 mg/kg methadone intravenously every 6 hours, 30 mg/kg of Unasyn intravenously every 8 hours, 10mg/kg of enrofloxacin intravenously given daily, metoclopramide given as a constant rate infusion at 2mg/kg/day, and Plasmalyte at a rate of 50 ml/hr to start, eventually decreased to 20 ml/hr. While at AERC, a chemistry panel revealed mildly increased liver values (ALT: 132, ALP: 314), and the amylase and lipase were markedly increased (AMYL: 1823, LIPA 5910). A snap PLI revealed an abnormal elevation. A FAST scan revealed moderate ascites, and a large, hypoechoic pancreas. While in hospital, a nasogastric tube was placed to facilitate enteral feeding. The nasogastric tube remained in place for two days, after which she was fed small amounts of a low-fat diet. Skipper was transitioned to oral medication and discharged on 8/31/2019. At the time of discharge, she was on the following medications: Cerenia 30mg daily, ondansetron 8mg given every 12 hours, pantoprazole 10 mg given every 12 hours, carprofen 25mg given every 12 hours, Entyce 36mg given every 8 hours, tramadol 50 mg given every 8 hours, and sucralfate 0.5 g given as a slurry every 8 hours. At this time, Skipper's physical exam was unremarkable, she was drinking and had a decreased appetite, she was not vomiting, and she had normal bowel movements.

Over the next few days at home, Skipper's owner noted that she remained lethargic and her appetite had not increased. She felt as though Skipper was having abnormal urination and that the color of her urine was orange to brown. Skipper's owner brought her to AERC on the morning of 9/4/2019; on presentation, she was icteric, with a notable skin tent and tacky mucous membranes. She had markedly elevated liver enzymes (ALP: 2300, ALT: 287), and her total

bilirubin was moderately increased (T. billi: 5.5). A urinalysis revealed 4+ bilirubin in the urine. On abdominal ultrasound, there was a focal mixed echogenicity cavitated mass that appeared to be associated with the pancreas. At this time AERC recommended Skipper be referred to MSU-CVM Internal Medicine.

On presentation to MSU-CVM, Skipper's primary physical examination revealed she was bright, alert, and responsive. She was of ideal body condition score with a weight of 10.9 kilograms. Her vital parameters were within normal limits with a heart rate of 88 beats per minute, a respiratory rate of 40 breathes per minute and a temperature of 101.6 F. On cardiac auscultation, she had a grade II, left sided systolic murmur. She had strong, synchronous distal pulses. Auscultation of her lungs revealed no crackles, wheezes, or harsh lunch sounds. Her mucous membranes were pink and tacky with a capillary refill time of 2 seconds. She had a prominent skin tent and was estimated to be 6-8% dehydrated. Her sclera were icteric on examination of her eyes. There was a palpable mass like structure in her cranial abdomen on palpation.

Pathophysiology

Pancreatitis in dogs is a potentially treatable and reversable condition, that can be broken down into three categories: acute, recurrent acute, and chronic.[8] Acute pancreatitis will be the focus of this paper and can be further differentiated depending on the effects it has on the patient. Acute pancreatitis can be considered mild or severe, fatal or non-fatal and can be further differentiated based on the systemic and local reactions it causes such as abscess formation.[8] The pathophysiology of acute pancreatitis has yet to be conclusively decided; however, it is thought to occur due to co-localization of pancreatic zymogen and lysosomal proteases with the acinar cells.[5] These activate an enzyme called trypsin, which leads to the activation of other pancreatic

enzymes.[5] When the activated pancreatic enzymes are released into the pancreas a local inflammatory response is mounted. Two of these enzymes, trypsin and chymotrypsin, lead to neutrophil migration into the pancreatic tissue, which has been noted to lead to necrosis.[5] At this point multiple cytokines are released, which will continue to stimulate and worsen the inflammation within the pancreas.[5] In severe cases of acute pancreatitis, this can lead to systemic vasculitis which may result in multisystem dysfunction, as well as the potential cavitary effusion.[5] In addition to this, there will be alterations in pancreatic circulation that further exacerbate inflammation. This is because there is a reduction in capillaries after acinar cell injury takes place; when this is severe, it can lead to necrosis or abscess formation within the pancreas.[5]

The list of potential etiologies of pancreatitis in dogs is long, and non-specific. A few of these potential causes are: dietary factors, hypercalcemia, hyperlipidemia, bile reflux, corticosteroids, drug-related, ischemia, reperfusion, infectious agents, and endocrinopathies. Acute pancreatitis is also thought to potentially have a hereditary predisposition in miniature schnauzers, miniature poodles, and terriers.[8] It is often cited that a low-protein, high-fat diet in dogs can lead to acute pancreatitis.[6] Overweight dogs are said to be at a higher risk of acute pancreatitis, which may be associated with abnormal dietary intake.[5] A retrospective study showed, dogs who had recent ingestion of unusual food items, such as garbage, were at an increased risk of pancreatitis as opposed to dogs that ate a higher intake of treats and snacks.[4] This could suggest that inappropriate food plays a larger role in development of pancreatitis rather than the fat/protein content consumed.

Pancreatic abscesses are most commonly a sequela to severe acute pancreatitis that has failed to completely respond with medical therapy. This is a rare complication in small animal veterinary medicine, that usually becomes a concern for doctors if severe pancreatitis is showing

no improvement in the first 5-7 days of treatment. Pancreatic abscesses are defined as a collection of pus and necrotic debris within the pancreatic parenchyma. It has been argued that an abscess must be septic; however, in contrast with human patients, most canine patients in the veterinary literature have sterile pancreatic abscesses.[1] Regardless of bacterial involvement the majority of these cases require surgical intervention. Prognosis for pancreatic abscesses is typically thought to be poor.[1] Prognosis for patients with acute pancreatitis shows mortality rates ranging from 27%-58%. These results, however, may be skewed due to the reports coming from referral centers, therefore, the cases are more than likely severe at presentation.[5]

Clinical findings associated with acute pancreatitis are generally rapid onset of anorexia, lethargy, abdominal pain, and vomiting.[7] The clinical signs at presentation can vary greatly depending on the severity of the disease process, and the level of dehydration that is present. Dogs can show signs such as polyuria, polydipsia, weight loss, diarrhea, a tucked-up stance, icterus, and in cases of pancreatic abscess formation, a mass may be palpable on abdominal palpation.[8] It is important to pay close attention to daily physical exam findings, as aggressiveness of treatment varies greatly depending on the severity of the disease process.

Diagnostic Approach and Consideration

After triage examination, a full diagnostic workup including abdominal and thoracic radiographs, abdominal ultrasound, cytology, and blood work were recommended. Thoracic and abdominal radiographs were performed under sedation. Thoracic radiographs revealed a small amount of pleural effusion, with the major consideration for this effusion being a modified transudate. Abdominal radiographs revealed decreased serosal detail throughout the abdominal cavity. Within the cranial to middle abdomen, there was an ill-defined, heterogenous, soft tissue opaque mass which was caudally displacing the small intestines. An abdominal ultrasound was

performed the evening of presentation, since ultrasound is the imaging modality of choice when diagnosing pancreatitis. It is important to note that ultrasonographic equipment and the skill of the person using the ultrasound play an important role in the sensitivity of this diagnostic tool.[2] In veterinary patients with pancreatitis, ultrasonographic findings usually include, an enlarged hypoechoic pancreas, increased echogenicity of the surrounding mesentery, and altered pancreatic echotexture.[2]

Skipper's ultrasound revealed a mild to moderate amount of echogenic free fluid within the peritoneal space. There was an ovoid, irregularly marginated hyper and hypoechoic mass that was heterogenous in echogenicity. It measured 2.8 x 3.7 x 4.6 cm and appeared to be associated with the gastric wall and the pancreas. The mass demonstrated blood flow on color Doppler and B-flow interrogation. The pancreas was diffusely enlarged, irregularly marginated, hypoechoic, and heterogenous in echogenicity. Portions of the pancreas demonstrated minimal blood flow on color Doppler and B-flow interrogation. The mesentery and omentum were diffusely hyperechoic and heterogenous, especially around the pancreas. Within the mesentery adjacent to the left limb of the pancreas, there were several variably-sized irregularly marginated anechoic structures that demonstrated acoustic enhancement. The abdominal lymph nodes were diffusely enlarged. Fine needle aspirates were taken of the mass, the mesentery, and the jejunal lymph nodes. Five milliliters of abdominal fluid were collected for assessment. The samples were submitted to the clinical pathology service, which revealed the abdominal fluid was an exudate containing 70% nondegenerate neutrophils. The mass was consistent with neutrophilic inflammation. Venipuncture was performed to allow evaluation of a complete blood count, a chemistry panel, a coagulation profile, and amylase/lipase send out test.

The complete blood count revealed a moderate neutrophilia (Segs: 22002, Bands: 506), a mild lymphopenia and monocytosis (Lymph: 759, Mono: 1770), and a moderate thrombocytopenia (Plt: 112). A chemistry panel revealed a severe elevation in Skipper's liver enzymes (ALT: 228, ALP: 3229), a severely elevated total bilirubin (t. bili: 2.6), a moderately low albumin and total protein (Albumin: 2.2, Total protein: 5.3), and a low anion gap (Anion gap: 6). Her coagulation profile was within normal limits. The most common clinicopathologic findings with acute pancreatitis are a leukocytosis, azotemia, and significant increase in liver enzymes.[5] An amylase and lipase of the peripheral blood and the abdominal fluid were sent off and came back within normal limits. In canine pancreatitis, serum amylase and lipase activities have shown to be increased; however, neither of these enzymes are specific to the pancreas because they also originate from the gastrointestinal mucosa and are excreted by the kidneys.[5] One retrospective study said that 15%-20% of cases of canine pancreatitis had normal serum lipase and amylase.[3] At this time, it was decided that Skipper would remain a patient of the Internal Medicine Department for treatment of acute pancreatitis with pancreatic abscesses.

Treatment and Management

Over the next 5 days Skipper was medically managed. She was initially started on Plasmalyte at 2 times her maintenance rate, which was a rate of 62 ml/hr to help correct her deficit. She was started on the following medications, 1 mg/kg Cerenia intravenously given daily, 1 mg/kg pantoprazole intravenously every 12 hours, 30 mg/kg of Unasyn intravenously every 8 hours, 10mg/kg of enrofloxacin intravenously given daily, 1 mg/kg of ondansetron intravenously every 8 hours, and she was started on a constant rate infusion of fentanyl at a rate of 2mcg/kg/hr. The main stay of treatment for pancreatitis is said to be a combination of fluid therapy, anti-emetic, proton pump inhibitors, and analgesia.[5] More recently research has reported

that in contrast to previous beliefs it is important to feed the patient early in the disease process.[5] This is because the gastrointestinal tract is now thought to be a major contributor to the systemic inflammatory state during acute pancreatitis, particularly if it is not supplied with luminal nutrients.[5] When feeding pancreatitis patients, it is important to know that enteral feeding is a better choice than feeding the patient with total parenteral nutrition, as studies have shown this to be harmful.[5] Although not used in Skipper's treatment, patients with pancreatitis can be treated with anti-inflammatory doses of prednisone, this is because they are known to counteract most all pathways of inflammation. Corticosteroids also inhibit proinflammatory mediators and decrease sequestration of neutrophils.[1] Since Skipper remained inappetent, a nasogastric tube was placed to facilitate enteral feeding. She was fed Royal Canin Low Fat liquid diet. The nasogastric tube had to be replaced three times and was therefore pulled on the third day of hospitalization. She was started on Entyce at 36mg given every 8 hours, sucralfate 0.5 g given as a slurry every 8 hours, and pentoxifylline at 100mg given every 8 hours. At this time a complete blood count and chemistry panel were performed and a recheck focal ultrasound was repeated. The ultrasound showed an unchanged abdomen from the ultrasound performed at presentation. The complete blood count reveled a mild anemia (HCT: 30.5), a moderate thrombocytopenia (platelets: 80), and moderate neutrophilia (segs: 22004). The chemistry panel revealed only mild changes from the panel performed at presentation. At this time in Skipper's treatment, due to her static condition despite days of appropriate medical therapy, it was decided to consult MSU-CVM Surgery Service for an exploratory laparotomy.

In preparation for surgery, Skipper was sedated for an abdominal computed tomography. This revealed within the region of the greater curvature of the stomach and the body of the pancreas an ovoid, smoothly marginated, fluid attenuating, rim contrast-enhancing structure that

measured 2.4 x 3.4 x 2.4 cm. There was a similar appearing smaller mass associated with the left limb of the pancreas measuring 2.4 x 2.9 x 0.9 cm. There were two more fluid attenuating smaller masses associated with the body of the pancreas. After the CT was interpreted, it was determined that Skipper should be taken to surgery for a pancreatic abscess omentalization. During surgery, a significant amount of fluid was noted in the peritoneal cavity. The stomach, pancreas, omentum, and transverse colon were all adhered to one another and covered in adhesions. The pancreas appeared enlarged, edematous, and had numerous necrotic foci throughout. The adhesions in the abdomen were broken down with sterile cotton swabs, the LigaSure and hemostats. Two areas of the pancreas were collected for histopathology submission. The mass was aspirated for culture and then cleaned out using a Frazier suction tip, and subsequentially flushed multiple times. An esophageal feeding tube was placed to facilitate enteral feeding post-operatively, and the position of the tube was checked with a lateral radiograph. During surgery, there was significant hemorrhage, so Skipper was given a blood transfusion and started on a constant rate infusion of norepinephrine at 0.5 mcg/kg/min. Post-operatively Skipper was continued on norepinephrine, a constant rate infusion of fentanyl at 5 mcg/kg/hr, a constant rate infusion of ketamine at 2 mcg/kg/min, and was continued on her previous medications. Her blood pressure was continuously monitored the night after surgery. Her norepinephrine was successfully tapered by midnight after surgery and her mean arterial pressure remained stable throughout the night. Over the next 5 days Skipper's ketamine and fentanyl rates were gradually decreased until she was able to be transitioned to an oral analgesic medication. Skipper was slowly fed through her esophageal tube for the next few days until she reached her full resting energy requirements. She was fed a slurry of a veterinary prescription low fat diet. Prior to discharge, a renal panel revealed improvement of her liver enzymes and her

hypoalbuminemia. She was discharged on Cerenia, ondansetron, and pentoxifylline. Although she had begun eating small amounts of food prior to discharge, she was given instructions on how to be fed through her esophageal feeding tube until her appetite was good enough for her to be consuming her full resting energy requirements by mouth. She was discharged after 14 days of hospitalization.

Case Outcome

At recheck Skipper was bright, alert, and responsive. She was underconditioned at a weight of 10.1 kgs. Her vital parameters were within normal limits with a heart rate of 84 beats per minute, a respiratory rate of 44 breathes per minute and a temperature of 101.8 F. On cardiac auscultation she had a grade II, left sided systolic murmur. She had strong synchronous distal pulses. Auscultation of her lungs revealed no crackles, wheezes, or harsh lunch sounds. Her mucous membranes were pink and moist. She was adequately hydrated, and no mass was palpable in the abdomen. Her complete blood count, and chemistry were within normal limits. She was sedated for an ultrasound, which revealed her pancreas to still be mildly enlarged and hypoechoic. Her mesentery was still hyperechoic; however, there was no free fluid within the abdomen. Skipper was discharged with instructions for her referring veterinarian to remove the esophageal feeding tube in 7 days.

Conclusion

Acute pancreatitis is a multifactorial disease that can be seen in the canine patient at different levels of severity. Pancreatitis is often thought to be due to hyperlipidemia, dietary indiscretions, and in some cases can have a heritable component. Patients should be treated quickly and aggressively for the best outcome. Treatment with intravenous fluids, anti-emetics,

proton pump inhibitors, analgesics, and enteral nutrition are the most common treatments for this disease. It is important for clients and practitioners to understand that severe pancreatitis can have potentially fatal sequelae such as pancreatic abscess formation, multi-organ failure, or necrosis of the pancreas. In cases such as Skipper's, referral, surgery, and extensive hospitalization and management may be necessary.

References

1. Cornell, Karen. "Pancreas ." *Veterinary Surgery: Small Animal*, by Karen M. Tobias, Vol 2, Elsevier/Saunders, 2012, pp. 1669–1670.
2. Cridge, Harry, et al. "Association between Abdominal Ultrasound Findings, the Specific Canine Pancreatic Lipase Assay, Clinical Severity Indices, and Clinical Diagnosis in Dogs with Pancreatitis." *Journal of Veterinary Internal Medicine*, 2020, doi:10.1111/jvim.15693.
3. C.S. Mansfield, B.R. Jones. "Plasma and urinary trypsinogen activation peptide in healthy dogs, dogs with pancreatitis and dogs with other systemic diseases: *Aust Vet J*, 78 (2000), PP. 416-422. (77)
4. K.Y. Lem, G.T. Fosgate, B. Norby, et al. "Associations between dietary factore and pancreatitis in dogs" *J.Am Vet Med Assoc,* 233 (2008), pp. 1425-1431. (41)
5. Mansfield, Caroline. "Acute Pancreatitis in Dogs: Advances in Understanding, Diagnostics, and Treatment." *Topics in Companion Animal Medicine*, vol. 27, no. 3, 2012, pp. 123–132.

6. M.D Yago, E. Martinez-Victoria, J.R. Huertas, et al, " Effects of the amount and type of dietary fat on exocrine pancreatic secretion in dogs after different periods of adaptation" *Arch Physiol Biochem,* 105 (1997), pp. 78-85. (38)
7. R.S. Hess, H.M. Saunders, T.J. Van Winkle, et al. "Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in dogs with fatal acute pancreatitis: 70 cases" (1986-1995) *J Am Vet Med Assoc,* 213 (1998), pp.665-670. (52)
8. Simpson , Kenneth W. "Diseases of the Pancreas ." *Handbook of Small Animal Gastroenterology*, by Todd R. Tams, W.B. Saunders, 2003, pp. 353–364.