Exocrine Pancreatic Insufficiency in a German Shepherd Dog

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Abstract

This case report describes the presentation, clinical signs, diagnostic evaluation and treatment of a three-year-old intact male German Shepherd Dog (GSD) that presented to the Cornell University Hospital for animals with a one-month history of diarrhea, light-color stools, lethargy and weight loss. Based on the dog's signalment, clinical signs and low trypsin-like immunoreactivity (cTLI) test, the dog was diagnosed with exocrine pancreatic insufficiency (EPI). Based upon serum levels of cobalamin and folate, the dog also had evidence of a small intestine bacterial overgrowth (SIBO), a common sequela of EPI in dogs. The dog was treated with oral pancreatic enzyme replacement, antibiotics, and cobalamin supplementation. The dog is currently responding well to treatment with a cessation noted in his major clinical signs (weight loss, diarrhea and lethargy).

Introduction

Exocrine pancreatic insufficiency (EPI) is a condition characterized by inadequate synthesis and secretion of digestive enzymes by the exocrine pancreas [1, 2]. This deficiency in pancreatic enzymes causes a syndrome of maldigestion and malabsorption resulting in yellowish or grey feces (steatorrhea), increased fecal volume and frequency, weight loss, and flatulence in nearly 90 percent of affected individuals [1, 2]. Other signs of EPI include borborygmy, polyphagia, and coprophagia [1, 2].

The most common cause of EPI in dogs is pancreatic acinar atrophy (PAA), an autoimmune disease that causes selective destruction of the enzyme-secreting acinar cells of the pancreas [3, 4, 9]. PAA is most common in German Shepherd Dogs (GSDs), which are the most common breed to be diagnosed with EPI (GSDs account for almost 70% of EOI cases)[1, 5]. In

GSDs as well as Rough-Coated Collies and the Eurasian Dog breed, PAA is inherited in an autosomal recessive manner [4-7]. Other causes of EPI include chronic pancreatitis and pancreatic neoplasia [1, 8]. While certain dog breeds (e.g., Cavalier King Charles Spaniels and Jack Russell Terriers) are predisposed to EPI due to chronic pancreatitis, this etiology of EPI is more common in cats and humans [4, 8, 10-13].

Maldigestion and malabsorption may result from multiple etiologies. Thus, identifying cases of EPI requires differentiating intestinal disease from pancreatic disease. Diagnosis of EPI is made based on history, clinical signs and results of pancreatic function tests[1, 2, 9, 14-16]. Serum canine trypsin-like immunoreactivity (cTLI) is the most diagnostic and most common test used in diagnosing EPI [1, 14, 16]. Other tests include fecal proteolytic activity and fecal elastase activity analysis [2, 15]. The mainstay of EPI treatment involves lifelong oral pancreatic enzyme replacement [1, 2, 22]. Prognosis for dogs with EPI is good with approximately 80 percent of dogs responding to treatment[17].

Case History

"Zeus," a three-year-old intact male German Shepherd Dog (GSD), presented to Cornell University Hospital for Animals' Emergency Service on August 8, 2008 for evaluation of chronic diarrhea, flatulence, and lethargy. For approximately four weeks prior to presentation, Zeus' stools had been voluminous and a "mustard-cream" color. He also had lost over seven pounds (nearly 10 percent of his body weight) during this period despite having what his owners describe as an "excellent appetite." Zeus's local veterinarian (rDVM) had treated the diarrhea three weeks earlier with diet modification and unspecified medications, however Zeus's signs failed to resolve. Moreover, the rDVM reported that Zeus had a slightly elevated alanine

transaminase (ALT). On August 8, 2008, Zeus vomited three times and subsequently returned to the rDVM for evaluation. Repeat blood work was all within normal limits (including his ALT). The rDVM performed a contrast gastrointestinal study (i.e., barium series) and did not detect an obstruction, however he believed that Zeus may have an abdominal mass based upon the presence of a soft-tissue opacity seen on abdominal radiographs. Prior to referring Zeus to Cornell, the rDVM administered Zeus a steroid injection.

Clinical Findings

On presentation Zeus was bright, alert and responsive with a body condition score (BCS) of 2/9. No abdominal masses were palpated, however due to Zeus' emaciated condition, his spleen was prominent within his abdomen. Light-color stool was recovered from the glove used to perform his rectal exam. The rest of his physical exam was unremarkable. The rDVM had also forwarded along Zeus' abdominal radiographs. After reviewing these films, the emergency clinician concluded that the "mass" that the rDVM had labeled on the films was Zeus' spleen, which was normal, but prominent given his thin profile. Thus, Zeus' problems included weight loss despite an excellent appetite, diarrhea/soft yellow stools, flatulence and lethargy. Despite his previous history, the rDVM never observed Zeus to vomit. Zeus also never vomited while at Cornell.

Differential Considerations

Given Zeus' signalment, clinical signs, and normal blood work (performed by the rDVM) exocrine pancreatic insufficiency (EPI) was suspected as the cause of his diarrhea, weight loss, and lethargy. Other differentials for his condition included inflammatory bowel disease (IBD),

gastrointestinal neoplasia, infectious causes of chronic diarrhea, hepatic failure, and hypoadrenocorticism. Given the normal blood work submitted by the rDVM (specifically euglycemia), diabetes mellitus was not on our differential list.

Laboratory and Ancillary Diagnostic Procedures:

Diagnostic tests were performed to determine if Zeus had EPI. Blood was submitted for canine trypsin-like immunoreactivity (cTLI) analysis, which is the most diagnostic test for the diagnosis of EPI in dogs [2, 14, 16, 17]. Serum cTLI measures serum levels of the pancreatic enzymes trypsin and trypsinogen that enter the blood directly from the pancreas. Since trypsin is not absorbed by the intestines, its serum levels are not affected by intestinal disease. However, trypsin is excreted by the kidneys, so it can be elevated in cases of renal disease[14]. Zeus' cTLI was 0.91 ng/mL (reference: 5-25 ng/mL), which was very low.

Small intestine bacterial overgrowth (SIBO) is a common sequela to EPI[1, 2]. It is hypothesized that this is a results of increased substrate for bacterial growth in the intestinal lumen and lack of bacteriostatic factors in pancreatic secretions[1, 2, 18, 19]. The elevated number of bacteria sequester dietary cobalamin while producing large amounts of folic acid which results in decreased levels of cobalamin and increased levels of folate, respectively, in the affected animals' serum[1, 2, 18]. Thus, blood samples were also collected to determine Zeus' serum cobalamine (vitamin B12) and folate levels. These tests revealed decreased cobalamin levels (166 pg/mLl reference: 175-550 pg/mL) and increased folate levels (21.4 ng/mL; reference: 4-13 ng/mL).

A minimum database (complete blood count, urinalysis, and blood chemistry panel) was conducted to rule out hepatic disease, hypoadrenocorticism and infectious causes of Zeus'

clinical signs. The results of his complete blood count were all within normal limits. His serum chemistry panel was relatively unremarkable, with mildly decreased levels of amylase (280 U/L; reference: 286-1124 U/L) and a mild hyperphosphatemia (5.5 mg/dL; reference: 2.8-5.3 mg/dL). Similar serum chemistry values have been reported in other cases of EPI, however they are unreliable and not diagnostic of EPI[20, 21]. Ketones were detected in his urine (15 mg/dL) which was attributed to Zeus' maldigestion and malabsorption of nutrients causing a negative energy balance and subsequent increased mobilization of lipids to meet his energy demands.

An abdominal ultrasound was performed to determine if Zeus had IBD, which could produce signs similar to Zeus' and is often present concurrently in dogs with EPI. The ultrasound would also be helpful in identifying gastrointestinal neoplasia if it were present and confirm the absence of an abdominal mass suspected by the rDVM. On ultrasound, Zeus' spleen was normal in size with a mild and diffuse mottling that was determined to be incidental by the radiologist. No other abnormalities were detected on the ultrasound exam.

A fecal flotation (ZnO_4 and sugar) and Giardia were performed to exclude gastrointestinal parasites as a cause of Zeus' maldigestion and malabsorption. No parasites were detected on any of these tests.

Treatment

Since EPI in GSDs is an autosomal recessive disorder, it was recommended that Zeus' owner have Zeus neutered to prevent this disorder from being transmitted to subsequent generations. Unfortunately, the owner declined this recommendation as Zeus had already sired two other "fine litters". Zeus was started on a commercially-produced oral pancreatic enzyme powder (Viokase-V®) that contained amylase, lipase and protease. His owner was instructed to

sprinkle 2 teaspoons of this powder on every meal to provide the pancreatic digestive enzymes that Zeus was no longer able to produce. Tylosin (750mg PO BID) was also prescribed to treat the SIBO, as pancreatic enzyme supplementation alone is not sufficient to correct this bacterial overgrowth[17]. Finally, Zeus was placed on cobalamin supplementation (1000mcg SC once per week for six weeks) as he was severely deficient in this vitamin.

Zeus was kept on his current diet. While dietary modifications have also been attempted as a treatment for EPI, the results are controversial[23-24]. Since the response of dogs to diet change is variable, this treatment method is used in dogs that are initially unresponsive to enzyme replacement alone[17].

Most of the pancreatic enzymes provided by oral supplementation are destroyed by gastric acid and, thus, a large percentage of supplemental enzymes do not reach the small intestine. In dogs that initially fail to respond to enzyme supplementation, H-2 blockers (e.g. famotidine, cimetidine) have been used with success to decrease gastric acid secretion and enable more of the enzymes to reach the small intestine[17]. Zeus was not placed on these drugs as part of his initial treatment regimen.

Prognosis

The prognosis for dogs diagnosed with EPI is generally rather good as the mean survival time (MST) of these animals is greater than five years[17]. In general, approximately 80 percent of dogs show some response to oral pancreatic enzyme replacement therapy. Almost half of all treated dogs show complete resolution of clinical signs. Nearly another 30 percent exhibit resolution of most of their signs including diarrhea and weight loss. Unfortunately, approximately 20 percent of animals fail to respond to treatment[17]. At this time, there is no a

priori method to predict an individual's response to treatment. In addition, 20 percent of dogs diagnosed with EPI are euthanized within the first year due to failure to respond to treatment or the cost of supplementation[17].

Outcome:

Although Zeus has not returned to Cornell for any rechecks, his owner reports that he is still on the pancreatic enzyme supplementation. Zeus has gained significant weight in the three months since he was discharged from Cornell and his owner reports that "she can't even see his ribs." Given the owner's concerns about the cost of supplementation, it has been recommended that Zeus try supplementation with a generic enzyme replacement product. If Zeus' clinical signs return, his owner has agreed to return to the Viokase-V® powder.

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