Patient ID: 314544
Patient: Whiskey
Species: Canine (Dog)
Sex: Male Neutered
Breed: German Shepherd
Age: 7 years 3 months 5 days
Weight: 76.9412 Lbs
Color:
Microchip Number:
Visit Start Date:

Owner of Animal:

Mangle, Elizabeth
1965 Gray-Wilmurt Road
Cold Brook New York 13324

Phone: 315-826-3172

Discharge Date: 12/15/21

Reason for Visit: Weight loss/ liver values elevated /EPI

Problem List/Diagnosis:
1. Predominantly hepatocellular, mixed chronic liver enzyme elevation
- Rule out chronic hepatitis (infectious vs immune-mediated) vs copper hepatopathy vs neoplasia (lymphoma or HCC) vs other
- AUS 12/15/21: mild diffuse splenic and liver nodules, cholestystomegaly with dependent movable debris
- 12/15/21 liver cytology: Marked copper accumulation in some hepatocytes, mild mixed inflammation suspected, mild vacuolar change (glycogen)
- 12/15/21: Chem: ALT 2084 U/L, ALP, 243 U/L, AST 193 U/L, T Bili 0.3 mg/dL
- 12/10/21: Chem 10: ALT 2315 U/L, ALP 282 U/L
- 10/15/21: Chem 17: ALT 1589 U/L
- 9/13/21 AUS: Normal abdomen
- 9/13/2021: Chem 10: ALT 1142 U/L, ALP 433 U/L
2. Historic exocrine pancreatic insufficiency
- Fecal smear 12/15/21: abundant fat droplets
- 12/15/21: Chem: Decreased lipase (10 U/L)
- 6/29/2021: Texas GI panel: Folate 10.7 ug/L (normal), TLI 9 ug/L (low normal), PLI <30 ug/L (normal)
- Responsive to pancreatic enzyme trial years ago
3. Chronic soft formed stool-- rule out secondary to poorly controlled EPI vs small intestinal dysbiosis vs inflammatory bowel disease vs neoplasia vs other
- 6/2021 to 12/2021: hyporexia, soft stool, and weight loss (recently gaining weight)
- 6/29/2021: Texas GI panel: Cobalamin 940 ng/L (elevated), owner reduced supplementation
4. Small intestinal bacterial dysbiosis
- Fecal smear 12/15/21: global decreased mixed bacterial population
- Rule out secondary to chronic enteropathy vs other

Diagnostics Today:
- Chem: elevated ALT 2084 U/L, ALP, 243 U/L, AST 193 U/L, TBili 0.3 mg/dL, decreased Lipase 10 U/L
- B12: pending
- TLI, fasted: pending
- AUS: mild diffuse splenic and liver nodules, cholecystomegaly (gallbladder dilation) with dependent movable debris
- Liver aspirate cytology: Marked copper accumulation in some hepatocytes, mild mixed inflammation suspected, mild vacuolar

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change (glycogen)
- Fecal smear: abundant fat droplets, global decreased bacterial population (mixed bacterial population)

Visit Summary:
Whiskey, is a 7 year old MN German Shepard, presenting to Cornell's Internal Medicine for evaluation of weight loss, chronic elevated liver enzymes, and historic EPI. On presentation, Whiskey was bright, alert, and responsive with normal vital parameters (temperature, heart rate, respiratory rate). He was slightly underconditioned (BCS 4/9, where ideal 5/9) and had mild diffused muscle atrophy. His teeth were all generally worn down. His abdomen was tense, but non-painful. He had foul-smelling feces on rectal exam, but rectal exam was otherwise normal.

Blood was collected for chemistry panel, B12 level, and TLI level. A fecal smear was evaluated. Whiskey was sedated for an abdominal ultrasound and liver aspirates.

Discussion:
Whiskey's liver values are stable from his last bloodwork. We will continue to monitor them and look for further evidence of synthetic dysfunction. His abdominal ultrasound showed a few splenic and liver nodules, however, this is non-specific and can be a variation of normal as dog's age. The aspirates of his liver also showed accumulation of copper in his hepatocytes (cells of the liver) with inflammatory cells. This is suspicious of a copper hepatopathy, which would explain the elevation in liver enzymes and Whiskey's clinical signs. However, a biopsy of the liver would be required to confirm this and differentiate from other liver diseases such as immune mediated hepatitis. Whiskey's fecal smear also showed abundant fat droplets which indicate that his EPI is not as well regulated as it could be. We would like to limit fat in his diet. Furthermore, we recommend a diet trial as Whiskey's chronic gastrointestinal signs and decreased bacterial flora could also be explained and potentiated by IBD (inflammatory bowel disease). The diagnosis of IBD would also require gastrointestinal biopsies. Because supplements often have proteins that can irritate the bowel and cause a flare-up of IBD, we recommend stopping as many supplements as possible (see instructions below). Please continue to monitor Whiskey's clinical signs at home; you have been doing a great job!

Medications:
Please discontinue the Proviable, Slippery Elm, and Denamarin, and B12 capsules for now

1. Tylan Powder- INCREASE to 1/4 tsp twice daily
2. Pancreatin 6X USP powder- Continue as previously prescribed (1tsp/cup of food)
3. Vitamin B12- Whiskey received a vitamin B12 injection today in hospital. **He will be due for another injection in one month on January 15th.**

Futher Discussion:
Copper hepatopathy
Copper-associated hepatopathy is a leading cause of chronic hepatitis in dogs, increasing in prevalence since 1997 when copper supplements in commercial dog foods were modified to a more bioavailable form. While the majority of research and literature available is in reference to Bedlington Terriers (these dogs have an identifiable genetic mutation resultin in hepatic copper accumulation), many other purebred and mixed-breed dogs of all ages also may develop copper-associated hepatopathy. More commonly and perhaps more severely affected are Labrador Retrievers; whether the high breed popularity influences this observation remains unclear. Doberman Pinschers, West Highland White Terriers, and some dogs related to Dalmatians also may develop profoundly increased hepatic copper concentrations accompanied by severe liver injury. A genetic cause has not been identified in any of these breeds. It is important to emphasize that copper-associated hepatopathy can be the primary cause of hepatitis in any dog (purebred or mixed breed) and can be definitively diagnosed only by liver biopsy. There is no recognized gender predisposition.

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Treatment of copper-associated hepatopathy requires copper chelation with concurrent restriction of copper intake from dietary and water sources. Dietary copper restriction can be achieved by feeding a prescription diet formulated for dogs. Administration of antioxidants is important, because copper induces liver damage through oxidative injury. Chelation therapy with d-penicillamine is the gold standard treatment. Response to treatment is ideally assessed via repeated liver biopsy, however this is generally not feasible in most patients and therefore monitoring improvement in hepatic enzymopathy is method by which treatment is assessed.

Vitamin E and biologically available SAMe are recommended antioxidants that also have anti-inflammatory and potentially antifibrotic effects. Vitamin C is contraindicated in copper storage hepatopathy, because it may foster injurious transition metal effects. After chelation therapy, it is essential to continue to limit copper ingestion in food and water lifelong. Adherence to a copper-restricted diet and water source may obviate the need for continual chelation or zinc therapy.

Inflammatory Bowel Disease

Inflammatory bowel diseases are the most common cause of chronic vomiting and diarrhea in dogs and cats. The term IBD is used to describe a group of conditions characterized by inflammation of the gastrointestinal tract and persistent or recurrent GI signs.

Inflammatory bowel disease (IBD) is a multi-factorial disease of dogs and cats characterized by chronic enteropathies that can significantly impact quality of life. These gastrointestinal diseases are usually thought of as being food responsive, antibiotic responsive, steroid responsive, or refractory, regardless of immunosuppressive therapies (idiopathic IBD).

Histologically, the small intestine, large intestine, or both can be affected. Lymphocytes and plasma cells are the most common cell infiltrates within the gastrointestinal (GI) tract, however other inflammatory cells can also be identified.

Although the exact etiologies of IBD are unknown, multiple factors can contribute to this persistent disease state. A confounding issue is that many healthy dogs and cats are exposed to similar factors relative to animals affected by IBD, but never become affected.

A clinical diagnosis of IBD is based on:

1. Presence of persistent (>3 weeks) GI signs
2. Inability to identify enteropathogens or other causes of GI disease
3. Histopathologic evidence of intestinal inflammation

A diagnosis of IBD is primarily one of exclusion and requires elimination of IBD mimics through complete clinical examination, laboratory testing, and specialized instrumentation. After the exclusion of infectious and parasitic agents, nongastrointestinal disorders, and intestinal structural abnormalities requiring surgery the most common diagnoses of chronic enteropathy include food-responsive enteropathy (FRE), antibiotic-responsive diarrhea (ARD), and idiopathic IBD. Definitive diagnosis requires histopathologic evaluation of biopsy specimens. The microscopic findings in IBD consist of minimal to pronounced inflammatory cell infiltration, often accompanied by varying degrees of mucosal architectural disruption.

IBD patients with mild to moderate clinical disease activity and normal serum albumin concentrations are first treated sequentially with dietary and antibiotic trials. If they fail to respond to either of these trials, immunosuppressive therapy is initiated. A positive response to a dietary trial allows the patient's disease to be classified as FRE, a term that includes both dietary allergy and intolerance. The primary option for a dietary trial is switching to a diet that leads to antigenic modification (eg, novel protein source, protein hydrolysate). The diet must be palatable and introduced in gradually increasing amounts over 4 to 7 days.In dogs with FRE, a clinical response is usually observed within 1 to 2 weeks of changing the diet. An antibiotic trial

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typically involves administration of tylosin or metronidazole. A positive response suggests ARD. The patient is typically maintained on antibiotics for 28 days. If signs recur after discontinuation of therapy, long-term antibiotic therapy is instituted with tylosin. Patients that do not respond to a diet or antibiotic trial are usually administered prednisolone or prednisone. However, as the side effects of glucocorticoids are usually more marked in large-breed dogs than in small breeds, adjuvant immunomodulatory therapy may be combined with glucocorticoid treatment for a faster taper period in dogs requireing long term therapy OR that do not tolerate glucocorticoid therapy.

FRE is highly prevalent among dogs with chronic enteropathies (at least 60% to 70%), and a favorable response to elimination or hydrolyzed diets within 2 weeks has been associated with a very good prognosis over 1 year after diagnosis. In these studies, the dogs were kept on the diet for at least 12 weeks after diagnosis before they were switched back to their original diet. In a recent large retrospective study in which all dogs with chronic enteropathy were sequentially treated, only 16% were suspected to have ARD. All ARD dogs relapsed shortly after discontinuation of antibiotics, making long-term management of these patients difficult. An additional decision-making factor may be the increasing problems with antibiotic resistance in dog populations. Also, evidence is accumulating that antibiotic treatment has long-lasting effects on the intestinal microbiome, which may lead to lasting dysbiosis that in itself could amplify intestinal inflammation. Many of these patients will eventually need steroids or other immunosuppressive treatments to control clinical signs.

A response to prednisone has been shown in up to 50% of dogs with chronic enteropathies. Other immunosuppressive therapies can be considered if more severe disease is present or severe side effects of steroids are anticipated. Many dogs and cats with chronic enteroapthies can have an excellent prognosis and live with an excellent quality of life with appropriate management.

Exocrine Pancreatic Insufficiency (EPI)
EPI is a disease characterized by a lack of pancreatic exocrine secretions into the small intestine. The most common causes of EPI are chronic pancreatitis (cats) and pancreatic acinar atrophy (dogs). The pancreas is responsible for secretion of enzymes that digest fats, carbohydrates and proteins. With insufficient enzymes, proper digestion will not occur, leading to the common clinical signs of large volume, malodorous diarrhea, weight loss, increased appetite, weight loss, and poor hair coat. This also leads to changes in the bacterial flora, contributing to clinical signs. The pancreas also secretes an enzyme called intrinsic factor which helps with the absorption of Vitamin B12. EPI is diagnosed by testing trypsin-like immunoreactivity (TLI). Treatment is usually successful with the addition of pancreatic extract to the food, Vitamin supplementation and a diet switch to a hydrolyzed protein diet that is low in fat. Although Whiskey's stool has improved, there were many fat droplets in his stool today. We recommend trailing a hydrolyzed diet that is lower in fat to aid in the control of this disease process.

Overview:
Your pet was seen by Dr. Kellie Riper of the Cornell Internal Medicine service today. Please allow for 24-72 hours for lab work results. If you have not heard from Dr. Kellie Riper within 96 hours please contact the Cornell Hospital for Animals at 607-253-3060. Please note that histopathology and send out laboratory requests can take longer. If you have not received and would like a paper copy of your lab work please contact the Cornell Medical Record department at the above number.

Instructions:
1. MEDICATIONS: As discussed, give all medications as directed. Please call Dr. Kellie Riper or your primary care veterinarian if you see any of the above mentioned side effects.

2. SYSTEMIC HEALTH: Please monitor for changes in systemic health including lethargy, vomiting, diarrhea, and poor appetite. Please call Dr. Kellie Riper or your primary care veterinarian if you see any of these signs.

3. FEEDING: **Please offer Whiskey the samples of Purina HA hydrolyzed diet**. Please transition slowly from his normal

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diet to avoid gastrointestinal upset.; give new diet: old diet in a ratio of 25:75 for 1-2 days, then 50:50 for 1-2 days, then 75:25 for 1-2 days, then 100:0 until otherwise directed. This diet contains 314 kcal/cup, so please feed him a total of 4.5 cups daily. It is imperative that during food elimination trials that no other treats or table foods be offered as this will interfere with response to diet. If Whiskey's appetite is reduced or he is not eating the HA well, you can top the food with a small amount of cooked tilapia or bison mixed with cooked sweet potato. It can take 4-6 weeks to fully assess a patient's repsonse to food elimination diet, however most patients will demonstrate improvement in 1-2 weeks.

4. FOLLOW UP: Whiskey requires a liver biopsy to diagnose the source of his chronic liver enzyme elevation and guide treatment protocol. **A drop off appointment has been made for Wednesday 12/22/21 at 2PM with Internal Medicine for recheck bloodwork and urinalysis prior to surgery the following day. Laparoscopic liver and gastrointestinal biopsies are scheduled for Thursday, 12/23/21 with the Soft Tissue Surgery Service.**

Thank you for visiting the Cornell Internal Medicine Service. Please call Dr.Kellie Riper if you have any follow up questions or concerns.

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