Nutritional Management of Copper-Storage Hepatopathy with Secondary Pancreatitis

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INTRODUCTION

Copper is one of the top three most plentiful trace elements in the body and plays an important role in regular metabolism.[1] Due to the ability to create reactive oxidation species, free copper is considered toxic. The liver is the most vital organ in regulating copper levels. It directly affects copper storage, metabolism, excretion through the biliary system, and reallocation of the element to other bodily tissues.[2] There have been certain recognized breed dispositions to develop copper-associated liver diseases..

The Bedlington terrier was the first breed in which hepatitis due to copper association was thoroughly studied. A genetic mutation was identified to be the source of the problem for this breed. Extreme copper values are apparent by 1 year of age and histopathologic evidence of copper accumulation are evident by 2 years of age in most affected dogs.[2,3] Bedlington terriers are not the only breed suspected to have primary copper-associated liver diseases (ex. Labrador Retrievers). Most other breeds though, develop some sort of hepatopathy from copper accumulation due to some secondary disorder. Cholestatic disorders are overrepresented in this category. Naturally, with an acquired issue in excretion of bile, bile quantities in the liver increase. As bile in the liver increases so does the concentration of copper since it is excreted through bile. Many breeds are thought to have this issue including, but not limited to, the Doberman Pinscher, West Highland White Terrier, Dalmatian, and both the Cardigan and Pembroke Welsh Corgis.[1,2,4,5,6,7,8,9]

The purpose of this report is to describe the presentation, diagnostic plan, treatment, nutrition plan, and outcome in a patient that presented with primary copper storage hepatopathy.

HISTORY AND PRESENTATION

Huck Boyd, an 8-year-old male neutered Pembroke Welsh Corgi, had elevated serum liver enzyme concentrations first noticed in February 2017 at his RDVM. ALT was 191 U/L (18-121 U/L). Shortly after, Huck exhibited increased thirst and urination. After that initial visit, Huck had recheck bloodwork performed in June 2017. ALT was 1627 U/L (18-121 U/L) and ALP was 531 U/L (5-160 U/L). An abdominal ultrasound was performed on June 15th, 2017, and showed a hepatic mass and chronic renal changes, including nephrolithiasis.

Huck was presented to Veterinary Specialty Services Emergency Care Clinic (VSS) on the same day for an abdominal exploratory and biopsy of the liver. Pre-anesthetic thoracic radiographs were unremarkable. An abdominal exploratory and liver biopsy were pursued the next day. The liver was observed to be small other than the right lateral liver lobe; the right medial liver lobe was biopsied and cultured. Huck remained hospitalized with observation of severe hyperbilirubinemia of 15.2 mg/dL (0-0.9 mg/dL) on June 18, 2017. Supportive therapy including cholestyramine was initiated; follow up ultrasound on June 22, 2017 showed a heterogenous, rounded and misshapen liver, severe pancreatitis with peritoneal effusion and a splenic nodule. The pancreatitis was probably the unintended result from manipulation and/or trauma of the pancreas during the surgical biopsy of the liver.

Recheck bloodwork on June 26, 2017, revealed that Huck remained hyperbilirubinemic with a bilirubin of 26.2 mg/dL (0-0.3 mg/dL). His liver values were increased with his ALT at 1011 U/L (18-121 U/L) and ALP 679 U/L (5-160 U/L) and hypoalbuminemia at 2 g/dL (2.7-3.9

g/dL). Leptospirosis serology was negative. Abdominal ultrasound was also rechecked and showed unchanged liver with right lateral hyperechoic "mass" observed histopathologically to be a regenerative nodule, unchanged severe pancreatitis, and increased peritoneal effusion with a heterogenous spleen.

Recheck bloodwork on June 27, 2017, showed a total bilirubin of 5.7 mg/dL (0-0.3 mg/dL), ALT 244 U/L (18-121 U/L) and ALP 314 U/L (5-160 U/L). Hypoalbuminemia had worsened to 1 g/dL (2.7-3.9 g/dL). Huck was discharged from VSS on June 27th, 2017, with therapy of Cerenia (24 mg q24h), codeine (3 mg tab, 1/4 tab q8h prn), mirtazapine (15 mg, 1/4 tab q24h), cholestyramine (3/4 packet in water q12h), ursodiol (100 mg q24h) and Pepcid (10 mg q12h). He returned on July 1st, 2017, for abdominocentesis (1700 mL removed) and was prescribed amoxicillin (250 mg q12h).

Huck had improved overall since his surgery, but was still decompensated compared to before his clinical signs first presented. He had another re-check appointment with VSS on July 11th, and he was reported to have a significant advancement in activity level and was described as 75-80% "better." Huck had bloodwork performed and he had hyperbilirubinemia at 0.9 mg/dL (0-0.3 mg/dL), ALT 396 U/L (18-121 U/L) and ALP 415 U/L (5-160 U/L). His owner was concerned about his conditions and how to manage it long-term. Huck had been eating a low fat Beneful lamb stew as well as lamb and rice dry food with vegetables and turkey breast treats. (Diet would later be changed). He had a good appetite with no vomiting. There was no diarrhea noted, and he presented with PU/PD, which had improved. D-penicillamine 125mg capsules POq12h and Vitamin E q24h were prescribed to go in conjunction with the cholestyramine, ursodiol, and Denamarin previously prescribed.

On July 12, 2017, histopathology results from Colorado State University as well as special stains had returned. Histopathology revealed moderate lymphoplasmacytic and suppurative hepatitis with single cell necrosis. Stains for copper showed a diffusely increased amount which was supported by extreme elevation in copper quantitation (20,600 ppm). Iron stains were mildly increased within macrophages and Masson Trichrome stain demonstrated mild increase in fibrous tissue with patchy bridging.

The diagnosis of copper storage disease was discussed with the owner in detail and chelation therapy also discussed. Bloodwork was rechecked that day and showed mild eosinophilia 2244 /uL (70-1490 /uL) on CBC and improved bilirubin 0.9 mg/dL (0-0.3 mg/dL) with improved elevation in ALT 396 U/L (18-121U/L) on chemistry panel. Hypoalbuminemia had resolved as well. Low dietary copper was recommended. For achieving that, a consultation with University of Missouri (MU) Veterinary Health Center Nutrition Service was pursued. He was still on his current medications at that time.

Dietary History

Huck's diet had recently been changed from Raw Primal rabbit and Acana fresh water fish with Hill's Hypoallergenic Treats to a homemade diet. His new diet consisted of a mixture of uncertain proportions of lean lamb (~10% fat by weight), brown rice, oats, carrots, peas, and a low-sodium lamb or chicken stocks. The diet was also mixed with Beneful. Declared treats that Huck received were organic pumpkin treats, lamb/rice treats, and Zukes wild rabbit treats.

Huck was on several supplements of unknown copper contents - AllerG3 (Omega 3), Cranberry Comfort Powder, Tumeric, B-12, and Platinum Performance Plus. Huck received his medication and supplements with foods. His food was divided into 2 meals and 2 treats per day.

He had a very good appetite and normally had moderate level of activity. Food allergies were claimed to manifest dermatologically with licking of paws and pruritus. Allergens articulated by Huck's owner were beef, chicken, turkey, pork, milk, corn, white potatoes, sweet potatoes, and Brewer's yeast. It is unknown whether his allergies were tested for or just determined by his owner.

Nutritional Assessment

The submitted consultation form listed body weigh at 11.4 kg (25 lbs.) and body condition score of 5/9 (where 1/9 is emaciated and 9/9 is severely obese). In dogs, an ideal body condition is defined as 4-5/9. Huck appeared then to be approximately at his ideal body weight and condition. However, muscle condition was reportedly reduced and may have been a consequence of Huck's liver condition and surgical biopsy complications.

Huck had a good appetite since being discharged and under his owners' care. He was described as an active dog that played for 2-4 times daily and for ~20 minute periods. He lived with one other Corgi. The description of Huck's current homemade diet was not complete in that foods included were varied in kinds and amounts. Hence, an accurate estimate of his caloric intake was precluded. Based on body weight and condition, age, and activity, Huck's daily energy requirement was estimated to be 650 kcal of metabolizable energy per day.

From a nutritional standpoint, the primary goal for Huck was to provide a nutritionally complete and balanced diet that was low but adequate in copper, appropriate for his listed dietary intolerances, and low in fat as an episode of pancreatitis was reported. Cause for the diagnosed nephrolithiasis was uncertain but could have been related to prior urinary tract infections; therefore, at that time a nutritional manipulation appropriate for the condition was not apparent.

Dietary Recommendations

In general, commercially prepared diets are recommended when an appropriate diet can be identified. Commercial diets compared to home-made diets have been preferred because they have been generally lower cost, higher palatability, more nutritionally consistent, less subject to ingredient drift, and are more likely to have passed a feeding trial. Commercial low copper diets are available, but they were unsuitable for Huck because these diets were moderate to high in fat and may contain ingredients that Huck's dietary history indicates may not tolerated, due to his allergies. Therefore, a homemade diet was recommended for Huck.

Diet recipe for "Huck" Boyd (enough for one day) Robert C. Backus, MS, DVM, PhD, Dipl. ACVN:

Custom ground lamb (10% fat): 130 grams, cooked weight.

-This is the principal protein and fat sources of the diet, adding flavor and palatability and meeting nutritional needs.

Rice, white, long-grain, enriched: 45 grams, dry weight. -
This ingredient provides energy and thereby allows the diet to be low in fat. White instead of brown rice is used because white rice is lower in fat.

Oatmeal: 52 grams, dry weight.
This ingredient provides energy and thereby allows the diet to be low in fat.

Carrots, chopped: 1/3 cup.
This ingredient provides vitamin A activity and fiber.

Soybean oil: 1/8 teaspoon.

This ingredient is added to meet essential fatty acid requirement. It is well enriched in the omega-6 essential fatty acid, linoleic acid, and does not add much fat to the diet.

Marine fish oil: 1/8 teaspoon.

Once the diet is found to be accepted and tolerated for at least 2 weeks, add this ingredient as a test of tolerance of the diet. Some dogs do not like fish oil. This ingredient is a source of long-chain omega-3 fatty acids which are nutritionally essential and have anti-inflammatory activities. One source can been found at

http://www.nordicnaturals.com/en/General_Public/Products_for_Dogs_&;_Cats/469

Low copper multivitamin-mineral supplement: "Balance IT ® canine - Cu", 7.5 grams.

This supplement is specifically formulated for dogs. It supplies essential minerals and vitamins not provided by the other ingredients. The supplement is formulated to be low in copper. The supplement may be purchased from the website

https://secure.balanceit.com/marketplace2.2/details.php?i=49&;cc=

Recipe is an enough for one day as it supplies 650 kilocalories per day. The nutrient content on kcal basis is protein 32%, fat 22%, carbohydrate 47%.

Treats:

Treats should be low in fat and copper and given to a limited extent (no more than 65 kcal/day). Good treats if accepted are slices of apples (~ 60 kcal/cup), carrots (~ 50 kcal/cup), and bananas (~ 130 kcal/cup).

Please note that foods used to give oral medications should be considered as sources of calories and if different from ingredients of diet they are potentially sources of undesired copper and fat.

The above diet was overall based on nutrient profile data of the ingredients, the diet was low in copper, approximately 4 ppm on a dry matter basis, in the range of recommended amount of dietary copper for copper hepatopathy. The fat content was low but more than adequate in essential fatty acids. Ingredients that were listed as being currently accepted and tolerated were used. Also, a low-copper vitamin/mineral supplement was used. It was strongly recommended that it should not be substituted. The supplement was specifically designed for use in diets made for dogs. Lamb and chicken stocks were omitted from the recipe because chicken was listed as a dietary allergen, copper contents were unknown, and need for enhancement of palatability of the diet was not demonstrated.

PATHOPHYSIOLOGY

Though copper is necessary for the body's normal metabolism it, like all heavy metals, has the potential to be toxic to the body.[1] The toxic potential of copper is due to the accumulation of too many free copper ions. These ions serve as a catalyst for hydroxyl radical formation. The hydroxyl radical products (OH^-) that are formed can cause oxidative damage to proteins, nucleic acids, and lipids directly.[3] In particular, they can cause notable morphologic changes in mitochondria & peroxisomes in liver cells, change the plasma membrane integrity, and damage lysosomal membranes leading to breaks and release of autodigestive enzymes which perpetuates further destruction.[1,5] The damage can lead to a vicious cycle resulting in abundant scar tissue formation and cirrhosis.

The organ that is most impacted by elevated copper levels is the liver. It has the highest concentration of copper compared to anywhere else in the body followed by the brain, heart, then kidneys.[1] There are 3 main ways in which copper can accumulate in the body. There can be just an increased consumption, abnormal absorption and/or storage with defective way(s) to excrete it (which is called primary), and cholestasis leading to abnormal excretion of copper (which is called secondary).[1] It is important to note that primary does not indicate that the only cause can be genetic but instead that the buildup of copper is the cause of liver injury.[5] Most commercial brand dog foods do not contain enough copper for increased copper ingestion to be the primary factor, but supplementation or excess copper in water sources can play a factor. However, it should not be completely ruled out until the dietary and supplemental status is fully known.

Copper's main access to the body is through ingestion. It can be found in drinking water, meat, nuts, seafood, and grain.[3] Nuts, shellfish, legumes, and unprocessed cereals are all high in copper, whereas dairy products, fresh vegetables, and fresh fruit are low in the metal.[1] Specifically, the upper small intestine is in charge of absorbing 40-60% of ingested copper.[3] The intestines absorb the metal via the apical membrane of its mucosa.[3] The unabsorbed copper is excreted with the feces.[10] Copper is absorbed by being carried by divalent metal transporter 1 (DMT1) an cooper transporter 1 (Ctr1).[3] Once the mineral reaches the blood, it is strongly bound to albumin or another protein and reaches the liver and kidneys in 2-6 hours.[3] Once in the liver, the copper can go in 1 of 3 places. It can be transported to other tissues for use via a glycoprotein produced by the liver, excreted out of the liver via bile, or stored inside the liver.[1,5]

If copper homeostasis is not maintained well, it initially starts from copper accumulating

in hepatic lysosomes, but as the excess overwhelms the lysosome, it overflows to the cytosol where it affects protein function, damages other organelles, and compromises the cell membrane. This leads to hepatocellular necrosis surrounding the central veins.[3]

DIAGNOSTICS

A simple blood chemistry can be informative if there is hepatocellular injury by looking at the indicators ALT and ALP.[11] While those markers can show the degree of overall damage to the liver, they do not reveal whether or not copper accumulation is the main culprit. Currently, a histologic examination of a liver biopsy with special stains such as rhodamine and/or rubeanic acid plus copper quantification are the only way to accurately diagnose copper storage hepatopathy.[1,3] Special care needs to be taken to avoid any damage to other abdominal structures when obtaining a hepatic biopsy.[1] A fine needle aspirate may be approached as well, but it is limited in that it cannot evaluate zonal copper distribution, grade of hepatocellular damage, or quantify the amount of copper in the sample.[2] Additional tests such as bile acids, ammonia tolerance, and PT/PTT can prove useful in ascertaining overall liver health but cannot definitively diagnose a copper storage disorder in the liver.

Two or more biopsy samples taken with a large core needle (14-16 gauge) are a necessary minimum in order to accurately quantify the degree of copper toxicosis.[2,3] It can be taken a variety of ways including percutaneously, via ultrasound guidance, laparotomy, laparoscopically, or via open abdominal exploratory.[2] It is recommended not to place the biopsies in formalin because the fluid contains copper and could possibly contaminate the

samples. Hepatic biopsies that are frozen or paraffin-embedded tissues can be used for copper quantification, but it is important to mention that the paraffin-embedded samples need a xylene extraction in order to be accurately assessed.[5]

Tissues should be collected in a leak proof container. Specifically, a rubber-free tube is the best choice as it avoids zinc contamination. They should also be shipped in a sealed bag inside of a leak proof container and maintained and a frozen or cold temperature during shipment. Once the sample is received, the liver biopsy needs to undergo specific stain(s) (rhodanine and/or rubeanic Acid) in order to accurately quantify hepatic copper concentrations because copper is not readily seen in routine stains.[1] Normal copper concentrations in the canine liver should be <400 ppm on a dry weight basis (DWB).[1] The amount of copper inside the liver that is required to cause damage is unknown, but hepatic copper greater than or equal to 600 ug/g DWB is commonly seen in dogs with hepatitis and >1,000 ug/g DWB is categorized as severe.[1,5] Other histologic evidence may present itself in varying degrees from focal hepatitis to cirrhosis depending on the disease stage.[12] Copper concentrations in the blood are typically unaffected, even with severe copper toxicosis so it is not usually not a useful diagnostic tool.[13]

While liver biopsies are the gold standard in diagnosing copper-associated hepatopathy, it is important to run a complete diagnostic workup in order to determine what is causing the abnormally high amount of hepatic copper. As mentioned earlier, there are 3 main ways in which copper can accumulate in the body. The first cause is that there can be just an increased consumption. To diagnose this, an accurate dietary and supplement assessment should be performed to confirm that quantity of copper given in the dog's diet and cholestasis leading to

abnormal excretion of copper (which is called secondary).[1]

The next cause is an abnormal absorption and/or storage with defective way(s) to excrete it (which is called primary). Primary copper-associated hepatotopathy is a breed-specific, autosomal recessive disease most commonly recognized in Bedlington terriers and first acknowledged in 1975.[1,5,14] The mutation that caused the problem has been determined to be a large deletion in the COMMD1 gene.[15] The COMMD1 protein connects with the N-terminus of ATP7B and is thought to promote the excretion of copper via the biliary route.[2] That deletion leads to eventual accumulation of too much hepatic copper, which in turn causes functional and morphological liver damage.[5] Bedlington terriers are also the only breed to have hemolysis due to copper release into the bloodstream noted.[3] To diagnose this type of hepatic disease in particular, one can look at a histologic sample of the liver (centrilobular accumulation with copper also present in other hepatocytes and within regenerative nodules) or perform a genetic test (one is commercially available for Bedlington Terriers).[3] Bedlington Terriers are not the only species that has a suggested mechanism of inheritance when it comes to copper storage hepatopathy. There has been evidence that Labradors, West Highland White Terriers, Dobermans, Dalmatians, Anatolian Shepherd Dogs, Corgis and mixed breeds have some genetic element involved in their developing copper-associated hepatitis.[1,2,3,5,16] The Labradors in particular, have 2 identified mutations (ATP7A & ATP7B) that are responsible for ~12% of total heritability when it comes to hepatitis from copper accumulation.[2]

The last cause of copper storage hepatopathy (cholestasis leading to abnormal excretion

of copper also called secondary) presents limited distinguishability diagnostically.[1] On histological examination, secondary copper accumulation is often restricted to areas adjacent to cellular injury.[3] Patients may present with clinical signs due to the inciting cause of the cholestasis such as weight loss, anorexia, vomiting, diarrhea, polyuria/polydipsia, jaundice, and even hepatic encephalopathy and ascites in severely affected animals. It is not a definitive diagnostic, but the onset of increased hepatic accumulation can be a significant (suggestive) differentiator between primary and secondary copper storage hepatopathy with the secondary form exhibiting clinical signs when a dog is more middle-aged to older. In Bedlington terriers, who have mainly the primary form, copper will start to accumulate between 6 months to 1 year of age with clinical signs developing soon after.[17] Labradors (which have primary, secondary, or both forms) exhibit clinical signs around 6 years of age which shows the delay of onset the secondary form can have when compared to primary.[2] It is important to mention that although currently cholestasis is the best reason currently understood as the cause there has been evidence to show that there might be other factors attributing to secondary copper storage hepatopathy. A study was performed where mixed-breed dogs had their bile-ducts experimentally ligated from 3 weeks to 93 days.[18] Hepatic copper concentrations of the dogs only increased if there was an excess of copper in the diet or an underlying copper excretion problem.[18] Those results give evidence that dogs are more resistant to copper overload secondary to cholestasis that previously thought.[18]

Prognosis for both primary and secondary copper storage hepatopathy is determined by the level of damage as well as the remaining hepatic function evident prior to treatment. Inflammation, whether caused by or in conjunction with copper accumulation, should be treated

with appropriate therapy, such as glucocorticoids, diet, Denamarin, S-adenosylmethionine, ursodiol, vitamin E. Unfortunately, fibrosis and cirrhosis of the liver are permanent. Prognosis of secondary copper hepatopathy is determined by the reversibility of the originating cause of the cholestasis and the degree of liver fibrosis/cirrhosis

TREATMENT/MANAGEMENT

Treatments for both primary and secondary copper-associated hepatopathy are aimed at minimizing free radical oxidation of tissues, decreasing inflammation, and decreasing the overall quantity of copper inside the body. Available treatments include dietary management, elemental zinc, ursodiol, Denamarin, chelating agents, glucocorticoids, and S-adenosylmethionine. Supportive care is also recommended, such as gastroprotectants, fluid therapy, appetite stimulation, and antibiotic therapy.

Simply put, the objective of medical therapy is to decrease copper absorption and increase its excretion.[3] An effective way to decrease absorption is to decrease dietary exposure. Most commercial dog foods meet or exceed National Research Council (NRC) minimums for copper. Unfortunately, for dogs that are prone to have excess copper storage, those values can be too large.[1] There are certain canine prescription liver diets meant to tackle this problem (Hills L/d and Royal Canin Hepatic Support).[5] They provide only ~0.1 mg Cu/100 kcal on a dry matter basis which coincides greatly with the recommended limit of 1.2mg Cu/100g of diet.[5,19] It is important to note that while appropriate dietary change decreases the amount of copper absorbed and reduces the rate of accumulation, it only has a minor effect on overall removal of copper from the body.[1]

Dietary supplements can also be part of adjunctive therapy. Ascorbic acid has been reported to decrease intestinal copper absorption when given with meals as well as possibly enhance excretion of copper through the urinary tract.[1] Elemental zinc causes the intestinal mucosal cells to produce metallothionein, a protein that has a high affinity for copper and, thus, binds dietary copper.[3] The copper is then excreted via the feces. Elemental zinc's speed in removing hepatic copper is rather slow so, it should not be a treatment by itself.[3] Elemental zinc has a 3 month administration minimum before it reaches therapeutic levels.[2] It also should not be administered with chelating agents, because that will cause a decrease in the efficacy of both.[3] With this information, it is clear that dietary management along with elemental zinc, while helpful, are better at prevention than overall treatment of copper-storage toxicosis.

There are multiple helpful hepatic medications such as ursodiol. Ursodiol is a bile acid that is useful for patients with cholestatic problems. The drug reduces cholesterol absorption and also thins the patient's overall bile acids and allows for better flow out of the liver resulting in decreased hepatic copper. There is also S-adenosylmethionine (SAM-e) which is found in the liver medication Denamarin. Both the SAM-e inside the drug and Vitamin E can help decrease inflammation and damage to the liver.[5] Glucocorticoids can be used by only if there is confirmed hepatocellular necrolytic or hemolytic emergencies.[5] Glucocorticoids can also stimulate appetite in dogs experiencing side-effect(s) from D-Penicillamine.[5]

One of the most important, if not the most important, therapeutic approaches to dogs with copper-storage hepatopathy is chelation. Chelation employs utilization of a soluble degradation product to bind with a metal to prevent it from causing damage and then be excreted with it. One

of the best copper chelators currently on the market is D-Penicillamine.[20,21] It reduces copper causing the metal to have decreased affinity for proteins and bind with the chelator instead.[5] The complexes formed are stable and are excreted through the urine swiftly.[5,22] Not only does it help eliminate the excess copper in the body, it has also been shown to have antifibrotic and immunomodulatory capabilities.[5] Furthermore, though D-Penicillamine does have some significant benefits, it is not without risk of side-effects. In ~30% of patients, gastrointestinal side-effects (vomiting, anorexia) are presented.[1] This can be managed by giving low-dose glucocorticoids.[1] It is recommended that the drug should be given on an empty stomach at least 20 minutes before a meal (food decreases absorption of the drug by almost 50%), possibly giving it with a little food could decrease the gastrointestinal upset.[1,5] Additional medications for liver failure or neutrophilic inflammation may be indicated based on results of hepatic function testing and liver histopathology, respectively.

CASE OUTCOME

Huck was diagnosed with primary copper-storage hepatopathy. After his biopsy, Huck had some difficulty recovering. He developed pancreatitis with peritoneal effusion which was possibly due to handling and/or trauma to his pancreas when attempting to get his liver biopsy. With time, medications, and supportive care Huck was discharged from the Specialty Clinic 12 days after his admittance. He was sent home on 1) ursodiol 250 mg, 1/2 tab PO q24h, 2) cholestyramine dissolve 3/4 packet in water q12h, 3) mirtazapine 15 mg, 1/4 tab q24h, 4) metronidazole 250 mg, 1/2 tab q12h, 5) amoxicillin 250 mg q12h, 6) Pepcid 10 mg q12h, 7) Cerenia 24 mg PO q24h, and 8) Denamarin 225 mg q24h.

Even with all these medications, patient still had an underlying problem. He needed to have a complete and balanced diet that was low in copper for his liver and also low in fat to not overstimulate his pancreas again. Desiring to find the right diet for Huck, he was referred to Missouri University's CVM Nutrition Department. No commercially available diet that was found. So, a complete and balanced homemade diet recipe was formulated specifically for Huck's dietary requirements. Since initiating his new diet with his medications, Huck has been doing well. He has been bright, alert, and responsive plus his ALT and ALP have gone down to normal levels on his blood chemistry. No signs of pancreatitis have returned as well.

CONCLUSION

While Bedlington terriers have become regular candidates for copper hepatopathy, it is important to remember that they are not the only susceptible breed. It is also important to know that any patient with sustained liver disease is at risk for too much copper accumulation. Copper hepatopathy is a chronic process with the patient presenting clinical signs only once the liver is at end-stage failure. Any animal with chronic liver inflammation or cholestatic hepatic disease should be considered for increased copper concentrations. If the clinician is suspicious of either one of those processes and within a susceptible breed, a liver biopsy is indicated. It can be difficult to treat copper-storage hepatopathy once it is categorized as either moderate or severe. As seen with Huck, it can be even difficult to manage their nutritional needs without perpetuating concurrent diseases. If identified early, however, specific dietary and medical management can enhance the quality of life for the patient and prevent further morbidity.

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