Chad’s Bad Jerky Experience

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Introduction

Fanconi Syndrome is a disorder that disrupts the functionality of the proximal tubule of the kidney. The impairment of the kidney causes amino acids, electrolytes, and nutrients to become lost in the urine instead of being reabsorbed into the body.[3] There are two types of Renal Fanconi Syndrome in mammalians: inherited and acquired. The inherited type of this disorder has been over represented in Basenjis, Norwegian Elkhounds, and “fancy silver” Cocker Spaniels.[3] The acquired condition of this disorder has been linked to ingestion of jerky treats, specific nephrotoxic antibiotics and metals, and kidney specific bacteria.[3,5,6] Patients have also been observed to have concurrent liver disease (ex. Copper hepatopathy) with the acquired condition of Fanconi Syndrome.[5,6]

Common clinical signs of Fanconi Syndrome include lethargy, weight loss, vomiting, diarrhea, poor hair coat, polyuria, and polydipsia.[1,2,56] Dogs have been observed to develop poor body condition scores as the disorder becomes a more progressive and chronic problem.[2] Progression of the disease can lead to patients becoming hyperchloremic with excessive loss of bicarbonate, which can develop into a metabolic acidosis and renal failure.[6,9] This disorder has also been seen to cause poor bone development in young dogs, but this is rarely documented.[2] With the impairment of the proximal tubules of the kidney, many solutes are lost into the urine and are unable to be reabsorbed. The tubule specifically loses the largest amount of glucose, bicarbonate, sodium, potassium, amino acids, and phosphorus.[3]

The diagnosis of Renal Fanconi Syndrome begins with the evaluation of a urinalysis and chemistry panel on the patient. This will determine if the kidney is losing solutes that it normally reabsorbs back into the body. The most common way of diagnosing Fanconi Syndrome is having glucosuria with a normal blood glucose level. Once a presumptive diagnosis of Fanconi

Syndrome has been established, the actual cause of the disorder is further investigated. This can be done by ruling out breed specific dogs that are predisposed to the inherited trait, performing blood tests to rule out kidney-associated bacteria (leptospirosis), evaluation of metal exposure, and a thorough history of patients' past medical drug prescriptions and antibiotics usage.[3,5,6]

To treat the inherited condition of Fanconi Syndrome, a specific diet protocol is designed. This diet focuses on aiding the body to make up for the solutes, minerals, amino acids and electrolytes that are lost by the kidneys.[3] The acquired condition is resolved by diagnosing and treating the primary cause of the kidney dysfunctionality. Prognosis for the inherited condition of this syndrome is good.[3] For the acquired condition, prognosis can range from good to excellent if treatment of the primary cause is resolved before chronic progression has occurred.[3]

History and Presentation

Chad is an 11 and a half-year-old, male neutered Jack Russel Terrier who presented to MSU-CVM Internal Medicine department on 10/3/19 due to suspected Fanconi Syndrome that was presumptively diagnosed by his referring rDVM. Chad originally presented to his primary veterinarian for having a two-week history of polyuria, polydipsia, and weight loss. Chad was evaluated on 9/24/19, where a CBC and Chemistry panel were performed. On 9/26/19 he returned to have a low dose dexamethasone test performed test for Cushing's disease which was then ruled out due to the test results showing normal limits. During this visit, Chad had an abdominal ultrasound and a urinalysis performed. The results revealed a urinary tract infection in addition to suspected Fanconi Syndrome. The abdominal ultrasound revealed his liver to be mildly heterogenous and echoic and anechoic areas in his gallbladder. This suggested a nonspecific hepatopathy that could be related or not related to his Fanconi Syndrome. The

primary veterinarian then suggested to begin Chad on a course of Clavamox and referral to MSU-CVM Internal Medicine department. Since starting the Clavamox, Chad's polyuria and polydipsia had improved. Chad had a history of being fed table scraps and multiple types of jerky treats throughout his life and his most recent jerky treat was approximately 6 days prior to presenting to MSU-CVM on 10/3/19. Chads previous medical history was seen to be within normal limits other than a mild elevation in ALT that was noted during a routine veterinary visit in 2016.

On initial presentation to MSU-CVM, Chad was anxious, alert, and responsive. He weighed 7.2kgs and had a body condition score of 5/9. His presenting temperature was 101.7° F, his pulse was 116 beats per minute, and his respiratory rate was 36 breaths per minute. Normal bronchovesicular sounds were noted on auscultation of the lungs, and no murmurs or arrhythmias were heard from the heart. His mucous membranes were pink and moist with a capillary refill time of two seconds. No nasal or ocular discharge was seen. Chad's ears were clean, and no inflammation was noted. His abdomen was shaved (due to his previous ultrasound at his primary veterinarian) and on palpation was tense, with no other abnormalities. There was no lymphadenopathy observed and the remainder of his physical examination was within normal limits

Diagnostic Approach

A recheck chemistry and urinalysis were performed on 10/3/19 and revealed marked hyperglycosuria in the face of normoglycemia. Additionally, a venous blood gas analysis revealed a mild metabolic acidosis, with a urine pH of 7.0. These findings confirmed the presence of Fanconi's Syndrome. In addition to mild hyperbilirubinemia, Chad's ALT and ALP

were found to be markedly elevated. An ammonia tolerance test was elected to be performed to evaluate Chad's overall liver functionality, and he was observed to markedly fail the test. These findings were supportive of a hepatopathy with secondary liver failure and it is possible that Chad's Fanconi's syndrome and hepatopathy could be separate problems.

A genetic test can be performed in patients that have inherited Fanconi Syndrome to rule out inherited or acquired.[3] An IgM Lepto Witness test was performed to rule out leptospirosis as the bacteria have been known to localize in the proximal tubules of the kidney and cause similar symptoms and clinical signs of Fanconi Syndrome.[3] Chad was observed to be negative for leptospirosis, therefore, it was ultimately recommended to obtain surgical liver biopsies or ultrasound-guided TruCut biopsies for histopathology and mineral quantification. Ultrasound-guided fine needle aspirates of the liver could be collected initially for cytology to evaluate for neoplasia.

MSU-CVM recommended for Chad to continue taking his Clavamox prescription and the Gonto Protocol (per Dr. Steve Gonto) be started to begin managing his Fanconi Syndrome. It was strongly suggested for Chad to no longer receive jerky treats. A recheck of Chad's Fanconi's syndrome and hepatopathy was suggested to be performed every 2 to 4 weeks with a urinalysis, blood gas analysis and chemistry.

Pathophysiology

Fanconi Syndrome has been linked as an inherited disease or an acquired disease. The cause of this syndrome's inheritance is due to an autosomal recessive trait. The inheritance

contributes to a defect in the proximal tubule of the kidney that prevents reabsorption of many solutes and electrolytes the body needs to keep at a normal equilibrium.

Acquired Fanconi Syndrome has been linked to multiple contributions that have a strong affiliation for the proximal tubule of the kidney. Specifically, pet jerky treats that originated from Asia (China and Japan) have been associated with high levels of melamine and cyanuric acid.[9] These two ingredients carry low levels of toxicity but when ingested together become synergistic for a more detrimental toxin.[4,9] Many of the acquired attributes have been specified above in the introduction section of this paper. In 2007, there was a recall of over 150 brands of pet associated foods that were linked to being contaminated with these chemicals.[9]

Melamine is a nitrogenic molecule when cyanamide is heated that is used in the development of many industrial uses; fire retardants, fertilizers, cooking appliances, manufacturing plastics, adhesives, cleaners, and yellow dye.[9] Cyanuric acid is a co-contaminant, intermediate product that is produced during the production of melamine.[9] This is used in the production of bleach, herbicides, and disinfectants.[9] Melamine and cyanuric acid are mild toxins that cause higher levels of toxicity when combined.[9] The chemicals combine in the kidney at their desired location of the proximal tubule and cause fine crystal formation in the shape of spheres.[4] These crystals cause a mechanical obstruction that prevents the reabsorption of many electrolytes, proteins, and nutrients.[4] When large amounts of crystals form in the kidney, the obstruction can cause compression of blood flow and begin killing cells of the kidney leading to renal failure.[4] As the proximal tubules become obstructed, bicarbonate is not able to be reabsorbed into the body which leads to renal tubular acidosis with alkalotic urine.[4,9] This also occurs when the blood results are seen to have many electrolyte abnormalities and increased levels in the urine. The kidneys should readily be reabsorbing glucose from the proximal tubule,

but when excess is being kept in the urine this leads to clinical signs of polyuria which, in turn, lead to polydipsia.

Treatment and Management

The mainstay of treatment for inherited Fanconi Syndrome is to use the Gonto Protocol. This protocol helps supplement the patient with essentials that the kidney would normally be reabsorbing instead of being lost due to proximal tubule dysfunctionality. Treatment for acquired causes of Fanconi Syndrome is achieved by using the Gonto Protocol as well as finding the primary threat and correctly treating the insult. The Gonto Protocol helps supply the body to correctly treat/protect the body from metabolic acidosis.[3] Diet will also help normalize the vitamin, electrolyte, and protein deficiency being caused by the kidney impairment.[3]

The Gonto Protocol consist of supplementing the patient with bicarbonate tablets BID, complete vitamin/mineral replacements BID (PET-TABS PLUS ADVANCED FORMULA), complete human vitamin weekly, Calcium/Phosphorus/ Vitamin D replacement BID (PET-TABS CALCIUM FORMULA), human complete body building amino acid tablet or teaspoon weekly (ex. Amino Fuel 1000), unlimited access to fresh water, high quality and protein dog food, and potassium supplementation BID (if patient is actively showing hypokalemia) (ex. Potassium gluconate tablets).[3]

Chad was continued on Clavamox BID for a week to finish out the prescription for treatment of his UTI. It was suggested to start Chad on the Gonto Protocol. Due to Chad having an unknown hepatopathy, it was recommended that he start a hepatic diet (ex. Hill's L/d) supplemented with a can of high protein "wet meat". Management of these causes are best performed by having the patient return every 2-4 weeks if patients venous blood gas, chemistry panel, and symptoms are severe. If the patient is less severe it is recommended to have

reevaluation of blood work every 8-10 weeks to ensure the protocol is adequately treating the patient appropriately.[3] Chad was recommended to be reevaluated in 2-4 weeks for his status of Fanconi Syndrome and find a diagnosis for his unknown liver disorder.

Case Outcome

On October 3rd, 2019, Chad was discharged from MSU-CVM Internal Medicine department after his previous diagnostics and recommendations were suggested. Chad has not since returned to MSU-CVM for progress of his Fanconi Syndrome and unknown hepatopathy. The primary veterinarian was contacted for an update on Chad's current status.

Chad returned to his primary veterinarian on 11/14/2019 for a recheck examination. It was observed that he had returned to his normal self and he has been urinating and drinking normally since his original visit/diagnosis. His diet was changed to a hepatic friendly diet and owner has been providing him supplement beef for protein. A CBC was performed and had a mild neutrophilia while on his chemistry the ALT and ALP were still moderately elevated. The rDVM suspects his chemistry to be related to infectious (bacterial cholangiohepatitis), inflammatory (hepatitis, cholangiohepatitis), or neoplasia. He prescribed Clavamox, Metronidazole, Denosyl and to return for a recheck visit in 2-3 weeks. A liver biopsy was suggested again to help diagnose his unknown hepatic disorder.

On 12/16/2019, Chad presented to his primary veterinarian for a reevaluation from his previous visit in November. Chad was noted to be lethargic, moaning, and having difficulty moving for over 2 hours. The owners said he was doing fine for 2 weeks after his previous visit on his new medication but was observed to not have his full appetite. After two weeks, the

owners observed Chad to become slightly lethargic and appetite dramatically decreased. The owners elected to stop giving Chad his medications in hopes he would feel better. He commenced a slightly better appetite but remained lethargic. The morning of his recheck visit, Chad became stiff and painful 2 hours before being brought into the clinic. He was noted to start walking again at the clinic but still appeared lethargic. Chad was eliciting pain to his abdomen and his thoracolumbar region of his spine. It was recommended that blood work be recheck and radiographs performed. Owner declined performance of diagnostics and was elected to prescribe Chad on Tramadol. The primary veterinarian suggested that Chad be referred to MSU-CVM for complete medicine work-up for his liver.

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