Polioencephalomalacia in a Bull

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Introduction

Polioencephalomalacia is a neurologic disease in ruminants caused by nutritional disorders. Polioencephalomalacia causes swelling in the brain and cerebral cortical necrosis[9]. Polioencephalomalacia is most commonly caused by a deficiency in thiamine or sulfur toxicity; however, it can also be caused by lead toxicity and water deprivation/ sodium toxicity.[5, 6, 9, 10] Clinical signs start subtle with depression, but they progress to cortical blindness with an absent menace and delayed PLR, head pressing, and opisthotos. [5, 6, 9, 10] These clinical signs can progress into seizures, ataxia, recumbence, comatose state, paddling, and eventually death. [5, 6, 9, 10]

History and Presentation:

Roll Tide is a 16 month old Black Angus bull that presented to MSU-CVM Food Animal Emergency Service on April 6, 2017 for unresponsiveness. He was previously purchased two weeks earlier at a sale, and was placed in a pasture of rye grass with cows. The owner brought him in on emergency due to being down and unresponsive in the pasture. At presentation Roll Tide was down in the trailer. Initial physical exam revealed 101.0°F, heart rate of 48bpm, and respiratory rate of 28bpm. With encouragement, he rose and walked in to the clinic. He was ambulatory but severely ataxic in all four limbs. Once in the stall, he head pressed against the wall and then collapsed into recumbency with minimal responsiveness. Further examination revealed an absent menace response, and a slow PLR response in both eyes. In summary, Roll Tide was blind in both eyes, had a slow PLR in both eyes, head pressing, had severe ataxia when ambulatory, and had become non-ambulatory and in lateral recumbency. The differentials at the moment were polioencephalomalacia, listeria, lead poisoning, hypovitaminosis A, and salt toxicity.

Initial treatment for Roll Tide that night included 17,500mg Thiamine intravenously (IV), 10,800mg LA-200 IV, 40mg Dexamethasone IV, and 1L of hypertonic saline IV. Also during this time blood was drawn to run a CBC and Large Animal Chemistry panel which only showed a mild neutrophilia and a lymphocytosis. This CBC along with the absence of a fever made listeria or a bacterial meningitis less likely. After the initial treatment Roll Tide became more responsive and was administered 4 gallons of oral fluids with 200mls of propylene glycol and electrolytes to correct his dehydration. Oral fluids were given because the catheter that was placed earlier failed and another could not be placed at the time. Based on clinical signs and lack of opportunities of lead poisoning in the history, and his rapid response to the thiamine treatment in the first 24 hours of treatment the top differential was polioencephalomalacia.

Pathophysiology/Anatomical Considerations

Thiamine deficiency is the oldest known reason for polioencephalomalacia to occur in ruminants. Ruminants generally do not acquire thiamine from their diet; instead it is synthesized from the microflora within the rumen.[12] Since the bacteria in the rumen produce the majority of thiamine requirements, ruminants are typically not affected when diets are inadequate in thiamine levels. However this high reliance on the rumen microflora means they are susceptible to low thiamine levels if an insult to the rumen occurs, such as, rumen acidosis due to grain overload, killing off a large percentage of the normal microflora.[12] Thiamine is present in the body as free base thiamine, thymidine monophosphate (TMP), thiamine pyrophosphate (TPP), and thymidine triphosphate (TTP).[3] TPP is an active form of thiamine. TPP is a coenzyme in several reactions in the Krebs cycle making it a vital component in the metabolism of glucose.[5, 8, 12] Thus, a decrease in the thiamine and its active forms will cause a decrease in in glucose metabolism and energy to vital organs like the brain. Consequently, this reduces lipid synthesis,

acetylcholine, and other neurotransmitter production in the brain, resulting in formation of clinical signs.[5] Another cause of decreased thiamine levels is an increase in thiaminase. Thiaminase is an enzyme that splits the thiamine molecule and irreversible deactivating it.[12] There are generally two types, Type I and Type II; the difference between the types is how they cleave the thiamine molecule deactivating it.[12] These enzymes can be found in several plants like bracken fern and horsetail.[6, 10] There are also several bacteria in the rumen, *Bacillus thiaminolyticus* and *Clostridium sporogenes*, that produce thiaminase.[8, 12] High grain diets, which risk rumen acidosis, also favor the growth of these organisms.[12] Therefore, diets that can quickly disrupt the microflora of the rumen (ie, feedlot or dairy setting), can induce polioencephalomalacia in cattle if the cattle are not properly acclimated. Amprolium is also another potential source of thiamine deficiency. Amprolium is a coccidiostat that works by being a thiamine analogue. It causes polioencephalomalacia by inhibiting the conversion of free based thiamine to the active form of TPP.[1] Studies have induced polioencephalomalacia in lambs when given large doses of amprolium.[1]

The other major way of causing polioencephalomalacia in ruminants is sulfur toxicity. With sulfur associated polioencephalomalacia, there is an increase in sulfide production in the rumen, more specifically hydrogen sulfide (H_2S) gas.[4] Sulfide is made in the rumen through two methods – degradation of amino acids that contain sulfur or the reduction of sulfur and sulfates to sulfide by bacteria.[2, 6] The bacteria that reduce sulfate in the rumen are categorized into two classes, dissimilatory and assimilatory. Dissimilatory bacteria reduce sulfate to sulfide; this sulfide will then either be absorbed in the blood stream or be used to form H_2S gas.[7] Sulfide can be neurotoxic when in high enough concentrations. It does this by inhibiting the mitochondrial sulfide oxidation at the level of cytochrome c oxidase.[5] This results in a decrease in ATP

production, meaning less energy for the brain causing cell death. Assimilatory bacteria also reduced sulfur, but they then use the reduced sulfide product in the formation of sulfur-containing amino acids.[6, 7] An imbalance in these bacteria with either an increase in the dissimilatory form or a decrease in the assimilatory form can cause an increase in rumen sulfide concentration leading to an increase in H_2S. Like with thiamine producing bacteria there are factors that affect these bacteria sulfur reduction ability like what sulfur compound is present, the diets composition, and the pH of the rumen. As the rumen pH decreases, the concentration of H_2S in the gas cap increases.[7, 11] H_2S is important because it is a way to measure and quantify the amount of sulfur in the rumen, and H_2S in high concentrations is toxic. During ruminant eructation, H_2S gas inhalation occurs, with resultant absorption in the lungs to the bloodstream. H_2S then travels via bloodstream to the brain where central neuron damage occurs by increasing oxidative processes generating free sulfite radicals that damage the neurons.[11] Besides its neurotoxic effects, sulfur and its derivatives can interfere with thiamine levels. One study demonstrated diets with a high sulfur content decreased the amount of thiamine passed through the rumen, through an increase in thiamine destruction and decrease in thiamine sysnthesis.[3] Sulfur can also bind magnesium (Mg). Mg is used to convert the thiamine into metabolically active TPP.[2] Thus, sulfur can cause polioencephalomalacia by either the neurotoxic effects of its reduced products, or inference with metabolism of thiamine into its metabolically active form of thiamine pyrophosphate (TPP).

Diagnosis

Getting a definitive diagnosis of polioencephalomalacia in a live animal is difficult due to unreliable test. The most common way to diagnose polioencephalomalacia in a live animal is to treat with thiamine injections and observe positive response.[5, 7] However, this diagnostic method

will not tell the underlying cause because both thiamine deficient cases and sulfur toxicity cases can respond positively to this treatment. There are some diagnostic tests that can be used to test for polioencephalomalacia with varied success. These include test blood thiamine levels, tissue thiamine levels, and fecal thiaminase levels.[5, 6] The problem with theses test are that they do not always decrease as expected in cases of polioencephalomalacia making them less reliable. In the outbreaks with suspected sulfur toxicity, measuring the amount of H_2S in the rumen gas cap can diagnose sulfur induced polioencephalomalacia.[11] If the H_2S levels in the gas cap are over 2,000 ppm then polioencephalomalacia is likely occurring.[6] In suspected sulfur toxicity cases, the feed and water supply should be test for high sulfur levels. High levels along with the clinical signs indicate polioencephalomalacia due to sulfur toxicity. Another test that can be performed is cerebral spinal fluid assessment. CSF will not diagnose polioencephalomalacia, but it can rule out infectious diseases like listeria and bacterial meningitis which can both cause clinical signs similar to polioencephalomalacia. Lead poisoning can also be rule out by testing the blood or rumen content for the presence of lead.

To definitively diagnose polioencephalomalacia a necropsy must be performed. On gross examination the cerebrum will be swollen and edematous, narrow sulci with flattened gyri, cerebral cortical necrosis, and a yellowish discoloration of the cerebrocortical gray matter that will autofluoresce under a black light.[5, 10] Histopathology will reveal degeneration and necrosis of neurons in the middle to deep cortical laminae and infiltration of macrophages in the areas of necrosis.[3, 10]

Treatment and Management

Treatment for polioencephalomalacia is a mixture of supportive patient care and thiamine supplementation. Depending on how clinical the patient is at presentation will determine the

success rate of treatment. Thiamine injections are the main therapy for polioencephalomalacia. The dose of thiamine is 10-20mg/kg given IM or SC every 6-8 hours. However, if the animal is showing severe signs at presentation, then the 1st dose of thiamine should be given IV.[4, 5] The thiamine is being given to either correct the thiamine deficiency that is causing the episode of polioencephalomalacia or to increase the amount of thiamine available to correct the sulfur toxicosis.[3] Thiamine also decreases cerebral edema, making it useful in treating lead toxicity. The other area that needs to be treated initially is the cerebral edema in the brain. Options to treat this are dexamethasone at 0.1-0.2 mg/kg given IV/ IM or 20% mannitol solution at 1g/kg given IV.[4, 5] An example of treatments and the treatment success is an outbreak of 18 steers from a 1000 head feedlot. These steers showed the neurologic signs of blindness, staggering and head pressing and were initially treated with dexamethasone and Resflor (combination of banamine and florfenicol). They later received TMS and thiamine injections. Out of the 18 treated, 14 responded and recovered to the thiamine injections. Nonsurvivors showed signs of polioencephalomalacia in the brain.[3] Since animals may become non-ambulatory and recumbent care should be taken to place the feed and water within reach. Also care should be taken if the animals are down as to what side they are on and if they are remaining on the same side they should be flipped to other side to prevent pressure necrosis form occurring.

Steps to prevent polioencephalomalacia due to thiamine deficiency are dietary. Avoidance of toxic plants like bracken fern, horsetail, and nardo fern which contain a thiaminase enzyme. To prevent polioencephalomalacia that is due to sulfur toxicity, avoid diets with high sulfur content like dried distillers grains.[5] When formulating diets for cattle the maximum dietary sulfur concentration is 0.4% of the dry matter consumed.[7] However, there are a number of outbreaks that occurred due to the water containing large amounts of sulfur, so the water should

be tested regularly to see what the sulfur concentration is, and then add that with dry matter to ensure the sulfur content of both is below 0.4%. Also slow acclimation to new diets that contain high grain rations is important. By slowly acclimating the diet, the rumen microflora is able to adjust and there is not the massive loss of normal flora that can occur with ruminal acidosis. Another prevention step is judicious uses of thiamine analogues like amprolium.

Case Outcome

The following morning, Roll Tide remained recumbent and the head pressing was less frequent. Physical exam did not reveal any new findings; his menace response was still absent in both eyes along with decreased PLR, and he was ataxic. His treatments for the day besides supportive care included 10,500mg of thiamine SC that morning and then the thiamine was reduced to 5,500mg SC every 6 hours, another 10,800mg dose of oxytetracycline, and 530,000 IU Vitamin E-AD injection IM. This was given because a rule out for blindness is vitamin A deficiency and vitamin E is an excellent free radical scavenger. The owner also called and updated the history. He confirmed there were not any batteries in the pasture further ruling out lead poisoning. However, he had fertilized the pastures with chicken litter a couple of weeks earlier. The chicken litter can cause polioencephalomalacia by disrupting the rumen flora due to the possible high mineral and carbohydrate content it can have. Thus, the most likely reason for Roll Tide's polioencephalomalacia is due to grain overload and ruminal microflora upset. On the third day of hospitalization, he was ambulating and quiet, alert, and responsive. He was no longer head pressing, but continued propulsive circling in his stall. His ataxia was less severe, his blindness continued with no menace and a slow PLR OU. His appetite improved with consumption of Bermuda grass hay and water. He continued to receive thiamine injections every 6 hours, his last does of oxytetracycline at 12,000mg SC, and his last dose of dexamethasone at

60mg IM. By the fifth day of hospitalization, Roll Tide had no head pressing or circling, and his menace and PLR was normal in OU. With a normal neurological status, Roll Tide was discharged with instructions to continue monitoring Roll Tide for improvement. If he or any other cattle on that pasture started showing signs of circling, head pressing, ataxia, or going off feed then they will need to be seen and treated for polioencephalomalacia. The owner was also instructed that when fertilizing a pasture with chicken litter again to spread it evenly, and let it set for 2-3 weeks before introducing cattle on it. Also he was instructed that when acquiring new cattle to keep the separate from the main herd for biosecurity reasons, but this also allows the new animal to be slowly acclimated to its new diet.

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