PEER REVIEWED

Case Report—Sulfur Toxicosis in Cattle caused by Corn Gluten Feed

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Abstract

An outbreak of sulfur toxicosis, with clinical signs and pathologic diagnosis of polioencephalomalacia (PEM), occurred in a case-lot of 150 crossbred, mixed-gender beef calves in northeast Georgia during May and June of 2009. Sixty head of cattle were clinically affected during a four-week period, with 35 of 60 cases resulting in death. Samples of feed, forage, and water were submitted for nutrient analysis. Sulfur concentration was 0.82% (8240 ppm) in the total mixed ration (TMR). Analysis of individual ration components revealed a sulfur concentration of 1.25% (12,500 ppm) in the corn gluten feed (CGF), while water samples had low sulfur concentrations (3.8 ppm). The sulfur content of the TMR was more than twice the maximum tolerable concentration of 0.40% of diet dry matter for cattle. Treatment was attempted with parenteral thiamine/B-vitamin complex and supportive care, with response rates reported as poor. The TMR was reformulated to non-toxic sulfur concentrations by reducing the percentage of CGF in the diet, reducing the daily feed intake, and offering supplemental forage, resulting in cessation of clinical cases.

Keywords: sulfur, sulfur toxicosis, PEM, polioencephalomalacia, corn gluten

Résumé

Une flambée d'intoxication au soufre, s'accompagnant de signes cliniques et d'un diagnostic de polioencéphalomalacie, s'est déclarée dans un groupe de 150 veaux de boucherie mâles et femelles de race mélangée dans le nord-est de la Georgie en Mai et en Juin 2009. Un total de 60 bovins ont été cliniquement affectés durant une période de quatre semaines parmi lesquels 35 sont morts. Des échantillons de nourriture, de fourrage et d'eau ont été analysés pour les nutriments. La concentration de soufre était de 0.82% (8240 ppm) dans la ration totale mélangée. L'analyse de certaines composantes de la ration a révélée une concentration de soufre de 1.25% (12500 ppm) dans le gluten de maïs des aliments alors que les échantillons d'eau contenaient une très faible concentration de soufre (3.8 ppm). La concentration de soufre dans la ration était deux fois plus élevée que la concentration maximale tolérable établie à 0.40% pour la matière sèche de la nourriture chez les bovins. On a essayé un traitement avec une administration parentérale de thiamine/vitamines du complexe B et des soins de soutien qui n'a pas été probant. La ration totale mélangée a été reformulée pour obtenir des concentrations de soufre non-toxiques en réduisant le pourcentage de gluten de maïs dans l'aliment, en réduisant la prise alimentaire journalière et en offrant du fourrage supplémentaire le tout mettant fin aux cas cliniques.

Introduction

Corn byproducts, such as corn gluten feed (CGF) and distillers grain with solubles, are a cost-effective and widely utilized source of protein and energy for beef cattle in the United States.[1,3] The majority of these byproduct feedstuffs are easily incorporated into rations as a primary ingredient in a total mixed ration (TMR) or utilized as a supplement for various classes of cattle on forage-based rations. In most cases, these byproducts are safe to feed in a TMR or in combination with free-choice forage. In the wet or dry fermentation processes, sulfurous or sulfuric acid, respectively, is used to maintain fermentation pH level. This additional sulfur (S), in the form of acid, increases S in a byproduct feed that would already contain moderate concentrations of S.[2,9] Yeasts used in the fermentation process also produce sulfites during their assimilation process, which contributes more S to the ration.[17] Batches of feed are often highly variable in the concentration of S they contain,[3,6,18] thereby making risk less predictable.

Clinical signs of sulfur toxicosis (ST) are dependent on dose (the concentration of S within the ration), duration (length of time in which appreciable concentrations are fed), state of sulfur-reducing ruminal microbes, and

form of S within the ration.[4,16] Subclinical ST often results in lost productivity due to decreased weight gain, decreased feed efficiency, and reduced dry matter intake, which is often elucidated during closeout.[3,8]

Clinical signs of ST that often result in the pathologic diagnosis of polioencephalomalacia (PEM) include blindness or visual impairment, anorexia, head pressing, bruxism, staggered gait, aggression, coma, and often death.[4,12,15] The previously listed clinical signs are not unique to ST. Other potential causes of cerebral neuronal necrosis, a synonym for PEM, are lead toxicosis, salt toxicosis, water deprivation, and thiamine-responsive PEM.[4,15] A key feature of all these diseases is their pathology to the brain, but a diagnosis of ST requires histological evidence of cerebrocortical necrosis, ancillary tissue diagnostics, and laboratory analysis of feed and/or water for elevated concentrations of sulfur.[10]

Case Description

During the fall and winter of 2008, approximately 150 crossbred beef steer and heifer calves from multiple auction markets were purchased and commingled into a single lot in northeast Georgia. The case-lot of cattle in this report represented one of several lots on the farm. Initial processing of the cattle occurred at the farm and included ear tagging, deworming, metaphylactic antibiotic,[a] and administration of a commercially available pentavalent modified-live virus vaccine.[b] The starter ration included free-choice grass hay and a concentrate feed containing a mineral pre-mix. After the initial receiving period, cattle were transitioned onto larger grass pastures and concentrate was provided in self-feeders or bunk feeders.

During the week of April 20, 2009, cattle were estimated to weigh an average of 700 lb (318 kg), and were moved from grass pastures with access to grower ration to a confinement lot in anticipation of shipment to a midwestern feed yard within two to three weeks. No signs of disease were seen prior to confinement. Feed intake of the grower ration (Table 1) was increased during the confinement period to an estimated 16 lb (7.3 kg) of dry matter per head. The lot contained multiple species of weeds, little residual grass, and no supplemental forage was provided. Approximately 10 to 14 days after confinement, the first case of neurologic disease was detected and cases continued to develop intermittently for 2.5 weeks, with 40 head affected and 25 cases resulting in death. Neurologic signs observed by the veterinarian included recumbency, blindness, convulsions, head-pressing, staggers, ptyalism, and facial tremors. Initial rule-outs included organophosphate toxicity, heavy metal toxicity, or other mineral toxicity. Thiamine-responsive PEM was a subsequent disease rule-out. Treatment of early cases was sporadic and non-specific, with poor response rates. Initially, the state transportation department's application of herbicide on a fence line surrounding the pen just prior to the disease epidemic was suspected to be the cause of the toxicity. Chemical toxicity caused by the herbicide was ruled out after chemical components within the herbicide were defined. Free-choice grass hay was added into the ration and cases subsided. Approximately three weeks after the initial cases, free-choice hay was discontinued from the diet, and within a few days signs of neurologic disease began to return as intake of the grower ration increased. Ten of the 20 newly affected cattle died. Hay was immediately returned to the ration, and the disease investigation was expanded to include the TMR. Shortly after the onset of the second outbreak of clinical signs, necropsy and toxicology results were obtained, and ration modifications were made.

Table 1. Calf grower ration fed during the disease outbreak.

Feedstuff	% DM	% sulfur in feedstuff	Sulfur (ppm)
Corn gluten	43.3	1.65*	7263*
Soy hulls	42.7	0.11[1]	469
Corn screenings	10.7	0.10[1]	107
Molasses	2.7	0.60[1]	160
Premix	0.7	3.61[2]	241
Analysis results	0.82[2]	8240 ppm	

[1]Estimated from National Research Council Beef 2000 Feed Ingredient Tables (not individually analyzed)
[2]Test results on premix (Michigan State University Diagnostic/Toxicology Lab)
*Corn gluten meal was not tested on the initial feed analysis. Extrapolated figures used to achieve 0.82% S concentrations found on feed analysis of suspect ration (University of Georgia Feed/Forage Lab)

Clinical Findings and Treatment

On May 6, 2009, the first physical examinations were performed on approximately 15 head showing various signs of neurologic disease. Several animals were recumbent and were humanely euthanized. Other calves were treated on the farm by the referring veterinarian, including thiamine/B-vitamin complex, oral fluids, and atropine. Variable treatment responses were seen; some cattle fully recovered, but others failed to respond and were humanely euthanized.

The second episode of the disease occurred about three weeks after the initial cases were seen, and corresponded with removal of hay from the diet. This outbreak was managed by feeding free-choice grass hay, and ration modification whereby the total S content of the ration was decreased. No systemic treatment was attempted.

Necropsy and Toxicology Results

On May 11, 2009, four mixed-breed heifers, approximately 12 months of age, were presented to the Athens Diagnostic Laboratory at the University of Georgia College of Veterinary Medicine for necropsy. The heifers were in good body condition with mild postmortem autolysis. Rumens contained liquid ingesta, and rumen papillae appeared blunted and atrophic. Multiple samples were taken for laboratory analysis. Histopathologic findings in all four cases were limited to the brain and rumen. These findings resulted in a diagnosis of PEM, and a secondary diagnosis of diffuse parakeratotic hyperkeratosis and mineralization of ruminal papilla. Lesions associated with listeria or rabies were not observed in tissue sections, but specific testing was not performed. Screening for toxic elements was performed on a subsample of the TMR. Toxic metal and organic compound screenings performed by gas chromatography and mass spectrometry were both negative. Mineral analysis performed by wet chemistry on the TMR indicated that copper, iron, zinc, and magnesium were in adequate ranges. The sulfur in this feed sample was 8240 ppm (0.82%). Sulfur concentrations in the mineral premix, forage grass sample, and water were 36,100 ppm (3.6%), 4060 ppm (0.41%), and 3.8 ppm, respectively.

Ration Modifications

The grower ration offered to the cattle during the disease epidemic included corn gluten meal, soy hulls, corn screenings, molasses, and a vitamin/mineral premix. The ration was initially reformulated when cattle were placed in confinement (Table 1) by increasing the inclusion rate of corn gluten meal, because of the increasing cost of corn. When sulfur toxicosis was suspected, the ration was modified to reduce the intake of sulfur. Table 1 provides the inclusion rates and sulfur content of the suspect ration offered during the disease break, and Table 2 shows the reformulated grower ration fed to reduce the S content in the diet.

Outcome

All remaining cattle in the case-lot were shipped to a midwestern feed yard for finishing in early September. Close-out information on the lot was not available. In summary, the case morbidity risk was 60 of 150, and the case fatality risk was 35 of 60, with 95 of 150 cattle marketed or shipped for finishing.

Clinical Relevance

The term PEM, or softening of the gray matter of the brain, can be defined in two different ways: 1) a histological brain lesion resulting in a pathologic di-

Table 2. Reformulated calf grower ration fed after diagnosis of sulfur toxicosis.

Feedstuff	% DM	% sulfur in feedstuff	Sulfur (ppm)
Corn gluten	25.5	1.25*	3187
Soy hulls	50.9	0.11[1]	560
Corn screenings	20.3	0.10[1]	203
Molasses	2.7	0.60[1]	160
Premix	0.7	3.61[2]	241
Analysis results		0.43*	4351 ppm

[1]National Research Council Beef 2000 Feed Ingredient Table (not individually analyzed)
[2]Not retested, results from earlier analysis
*Analysis results from University of Georgia Feed/Forage Lab

agnosis lacking etiologic specificity, or 2) a neurological disease syndrome often associated with altered thiamine status.[4] Ideally, the histological diagnosis of the lesion should be reserved for PEM.[4] Often the terms "polio" or "brainer" are used to describe clinical signs of various diseases that are most often thought to be associated with altered thiamine status. Based on clinical signs, a tentative diagnosis is made, and the animal is treated. In reality, the clinical signs associated with various disease processes that contribute to the histological PEM brain lesions are all very similar, but each has a different underlying cause. Therefore, considering other possible disease processes rather than just thiamine deficiency is important.

Sulfur is an important component of amino acids. In the ruminant, methionine can be used to synthesize all sulfur containing compounds except biotin and thiamine.[14] Rumen microbes can utilize inorganic S to synthesize organic S-containing compounds, which are then utilized by the animal.[14] Ruminal bacteria play an important role in the metabolism of S. Sulfur reducing bacteria (SRB) are classified by the manner in which they utilize S; some assimilate S into compounds that can be utilized by the animal, including amino acids and other organic molecules, while others dissimilate S and utilize it in their own energy production.[8] This process of dissimilation produces excess sulfide ions, and these SRB are responsible for the reduction of sulfur to hydrogen sulfite and hydrogen sulfate.[8]

Often, cattle exhibiting clinical signs of ST are treated based upon clinical signs that result from damage to the central nervous system (CNS). Sulfur-induced PEM is a disease primarily affecting the CNS, and clinical signs are thought to occur from two primary mechanisms, but the pathogenesis of this toxicity has not been completely elucidated.[3] First, reduced mineral bioavailability is thought to occur due to various complexes formed from the reduction of organic S or sulfate. This may serve to reduce performance and immune function and predispose cattle to a greater risk of secondary diseases.

Second, excess S in the ration is reduced to sulfide or hydrogen sulfide (H_2S) in the rumen, which is then absorbed across the rumen wall or inhaled following eructation.[8] Elevated concentrations are thought to occur when various forms of inorganic sulfate are made bioavailable by reduction to sulfide by sulfate-reducing bacteria. As high concentrations of H_2S continue to build up in the rumen gas cap, eructation occurs. Direct inhalation, following eructation, hypothetically enables the hydrogen sulfide to be taken into the lungs, absorbed into the blood stream, and exert toxic effects on the ruminant's nervous, circulatory, and respiratory systems.[3] In addition, these toxic concentrations of H_2S are no longer thought to be subject to the potential detoxification pathways in the liver that they would normally encounter if absorbed across the wall of the rumen into the bloodstream. This limits the oxygen-carrying capacity of the blood, damages a variety of key enzymes, and severely affects oxidative metabolism. The reduction in oxygen and ATP production results in toxic effects on the CNS. Therefore, sulfur-induced PEM appears to be directly mediated by the metabolized products from the reduction of S or sulfate, versus thiaminase-induced PEM that occurs as a consequence of the direct cleavage of thiamine.[3] Both of these mechanisms are important, and based upon the concentration of toxicity, can result in death or decreased growth and reproductive performance.

An interesting observation found during necropsy of each animal was chronic, subclinical acidosis in conjunction with the PEM. It appears that a more acidic condition favors a large rumen gas cap, which predisposes cattle fed a high-concentrate diet to potential toxicity.[4] In this case, increasing the amount of forage within the diet would have increased rumen pH and provided a feed source lower in S. With increased consumption of forage, there should subsequently be decreased proportional intake of TMR.

Sulfur consumed by the animal comes almost exclusively from two primary sources–feed (forage and concentrate) and water; both of these sources can be highly variable, and each must be considered in ration formulation.[3,5,7,19] Although Lamm[10] found that feed represents the most common source of toxic concentrations of S, an error in formulation of mineral premix should also be considered. Recommended dietary concentrations for most ruminants range from 0.18% to 0.24% of dry matter for microbial growth and microbial synthesis of S-containing compounds for the ruminant.[13] Maximum tolerable concentrations of S are 0.30% for high-concentrate rations (less than 15% forage) and 0.50% for high-forage rations (greater than 40% forage).[13] Live animal performance indicators such as average daily gain, feed efficiency, and dry matter intake have been shown to decline at sulfur concentrations greater than 0.30%.[11,20] Therefore, the risk associated with byproduct feeds containing high concentrations of S must be understood by the producer, and a significant margin of error must be allowed when feeding high and variable concentrations of sulfur at any stage of production.[3,16]

Conclusions

Sixty of the 150 head were clinically affected by the high concentration of sulfur in the TMR, with 35 of the cases resulting in death. High concentrations of sulfur in the TMR and a lack of a forage source to offset toxic concentrations of sulfur resulted in clinical cases of PEM that responded poorly to treatment. This

case demonstrates the need for communication between the producer, veterinarian and/or nutritionist, and the byproduct feed manufacturer. Testing the by-products or providing an appropriate margin of safety in ration formulation to account for the highly variable concentrations of S in loads of feed from production facilities is important. Producers and manufacturers must develop standardized forms of communication to ensure the safety and quality of their byproduct feed. As this case demonstrates, the inherent variability of sulfur concentrations in byproduct feed poses significant risks to producers who are uninformed and do not provide adequate margin of error in ration formulation.

Endnotes

[a]LA-200, Pfizer Animal Health, New York, NY
[b]Vista 5 SQ, Intervet/Schering-Plough Animal Health, De Soto, KS

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INFORMATION

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