PEER REVIEWED

Case Report - Polioencephalomalacia in Dairy Calves

Kathleen Emery, *DVM;* **Garrett Oetzel,** *DVM, MS*
Food Animal Production Medicine, Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin, Madison, WI 53706

Abstract

Polioencephalomalacia (PEM) is a neurologic condition in ruminants that can be caused by several dietary factors including water deprivation-sodium ion toxicosis, lead poisoning and high sulfur intake. Three month old calves on a 1500-cow dairy experienced neurologic problems during three separate episodes. The morbidity rate approached 75% each time. Based upon post-mortem examination, three of the affected calves were diagnosed with PEM. The history revealed a change in the formulation of the pelleted feed four days prior to the initial outbreak. Wet chemistry analysis of the pelleted feed revealed a sulfur content of 0.56% (dry matter basis), which was considered to be the cause of the PEM outbreak.

Résumé

La polioencéphalomalacie (PEM) est un désordre neurologique chez les ruminants qui peut être causé par plusieurs facteurs alimentaires incluant l'intoxication au sodium suite à une privation d'eau, l'empoisonnement au plomb et une prise élevée de soufre. Des veaux de trois mois dans une ferme laitière de 1500 têtes ont montré des signes neurologiques lors de trois épisodes différents. A chaque reprise, le taux de morbidité a atteint près de 75%. Suite à l'examen post-mortem, trois des individus affectés ont été diagnostiqués avec la PEM. Une enquête a révélé un changement dans la formulation des aliments comprimés quatre jours avant le déclenchement des problèmes. Une analyse chimique des comprimés a révélé un contenu en soufre de 0.56% (en matière sèche) qui a été considéré comme étant le facteur déclenchant le problème de PEM.

Introduction

Polioencephalomalacia (PEM) is a neurologic disorder of ruminants characterized by necrosis of the cerebral cortex. In certain regions of the world, PEM is also known as cerebrocortical necrosis. These descriptive terms refer to histologic lesions of the brain in which the gray matter (polio) of the brain (encephalo) undergoes softening (malacia).[6] The term PEM is frequently used to refer to a syndrome caused by altered thiamine status, however, numerous studies on the pathogenesis of PEM have not produced conclusive evidence that an overt thiamine deficiency is involved.[14] PEM is actually a histopathological diagnosis that can result from several causes, including acute lead poisoning, water deprivation-sodium ion toxicosis, high sulfur intake or severe ruminal acidosis. PEM is no doubt triggered by progressive thiamine deficiency in the field, however, more recent reports suggest a causal relationship between high sulfur intake and PEM.[5]

Early clinical signs of PEM include profound depression, anorexia and bilateral cortical blindness with intact palpebral and pupillary reflexes. A dorsomedial strabismus is frequently seen, as well as head pressing and odontoprisis.[13] Ataxia and proprioceptive deficits are apparent if the animal is able to walk. Severely affected animals become recumbent and may develop opisthotonus and signs of central vestibular disturbance, including a variable nystagmus, ventrolateral strabismus and head tilt.[3] Seizures or coma are likely to follow and untreated cases may die within 24 to 96 hours due to respiratory failure. The major differential diagnoses include lead poisoning, water deprivation-sodium ion toxicosis, meningitis, rabies, hepatoencephalopathy, enterotoxemia type D, and elevated sulfur intake.[2]

Case History

Three-month old calves in a 1500-cow Holstein herd in Wisconsin were experiencing neurologic disease. Calves were individually raised in five greenhouse barns housing 50 to 60 calves each. Calves were weaned from a commercial milk replacer at 45 days of age, at which time they were adaptated to a complete pelleted feed

over a two-week period. At any given time, there were approximately 75 calves in the 3-month age range on the farm. Based on farm records, the daily intake of pelleted feed was 6 to 8 lb/calf/day. Water was available *ad libitum* during the year, except in the winter months when it was offered twice daily. Calves remained in the greenhouse barns until they were moved into group housing at 4 to 6 months of age.

On November 24, 1999, caretakers observed neurologic signs in 50-75% of the 3-month old calves in one greenhouse barn. Calves were afebrile, and clinical signs included depression, varying degrees of blindness, head pressing, elevated respiratory rates and hyperesthesia. All affected calves were treated with vitamin B complex (500 mg IM), dexamethasone (16 mg IV), oxytetracycline (800 mg IV) and flunixin meglumine (200 mg IV). Several recumbent calves were given 3 liters of Lactated Ringer's Solution intravenously. Four calves died during this initial episode. A post-mortem examination was performed on one calf and tissues were sent to the Wisconsin Animal Health Laboratory in Madison, WI. The pathologist reported a presumptive diagnosis of bacterial meningoencephalitis. Additionally, sodium levels were elevated in the cerebral spinal fluid (CSF).

Calves were markedly improved by the following day. Cerebrospinal fluid was collected from two recovered calves and submitted to Marshfield Laboratories, Marshfield WI. Analysis revealed an increased number of white blood cells in the cerebrospinal fluid, suggesting meningitis/meningoencephalitis. The predominance of mononuclear cells in the CSF was suggestive of infection with *Listeria monocytogenes* rather than *Hemophilus somnus*, where neutrophils tend to predominate. The herd veterinarian recommended daily treatment of all calves with oxytetracycline and vitamin B complex for five consecutive days.

A second outbreak of neurologic disease in 3-month old calves occurred in another greenhouse barn on December 3, 1999. Clinical signs were similar to those seen in the previous episode, with approximately 75% of the calves affected. Those calves showing clinical signs were treated similar to the first group. Two days later, two calves not responding to treatment were euthanized. Brains were removed from both calves and sent to Marshfield Laboratories for pathological and cytological examination. Histological changes in the tissue were consistent with PEM. Mononuclear cell pleocytosis in the CSF was consistent with listeriosis, however, no microorganisms were isolated.

On December 17, 1999, a group of three month old calves in another greenhouse began showing neurologic signs. All calves were treated as in prior episodes. Two calves were referred to the Veterinary Medical Teaching Hospital at the University of Wisconsin-Madison for evaluation.

Clinical and Pathological Findings

Complete physical and neurological examinations were performed on each calf. The first calf was ataxic, the respiratory rate was slowed and the calf showed signs of depression and episodes of head pressing. Other neurological signs included blindness with dorsomedial strabismus, and lack of a bilateral menace response and palpebral reflex. The calf was humanely euthanized.

Necropsy examination revealed no gross lesions within the abdominal or thoracic cavities or joints. The cerebral cortices had areas of slightly swollen gyri and one area of slight depression. When sectioning the cerebrum, segmental areas of mild to moderate yellow discoloration were observed in the cortical grey matter (Figure 1). Ultraviolet illumination of sections of the brain revealed marked segmental areas of auto-fluorescence in the cerebral cortex, and bilateral symmetrical fluorescence within the thalamus (Figure 2). The presence of

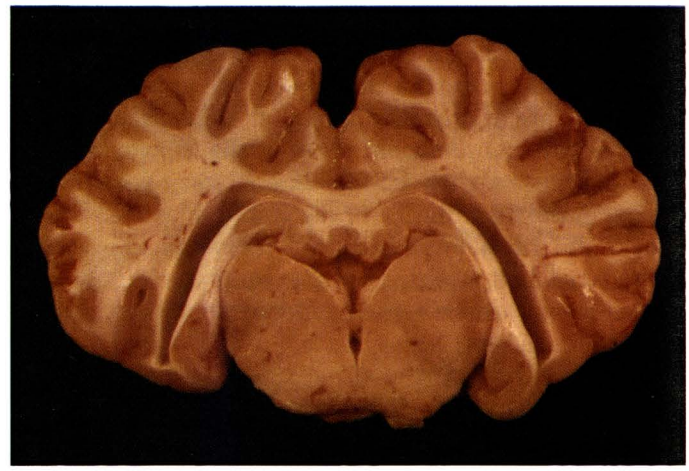

Figure 1. Xanthochromasia within the grey matter.

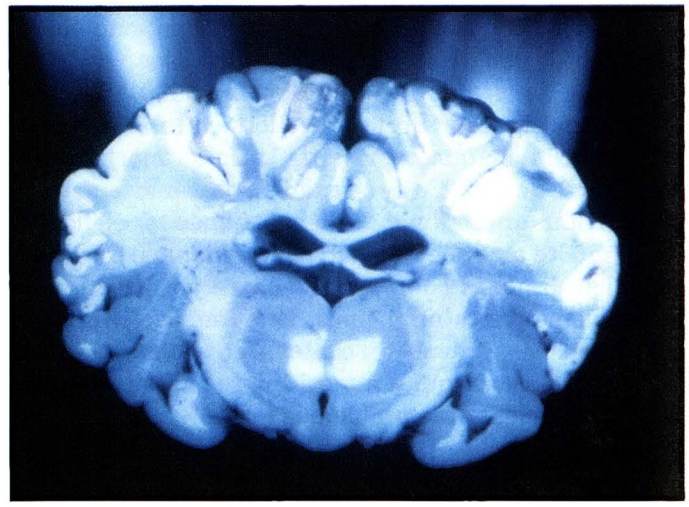

Figure 2. Autofluorescence of ceroid lipofusion in the cerebral cortex.

segmental xanthochromasia and auto-fluorescence within the grey matter of the cerebral cortex provided strong evidence for the preliminary diagnosis of PEM.[9]

Multiple sections of the cerebral cortex were examined histologically. Segmental areas of the cerebral cortex, thalamus and hippocampus had acute neuronal necrosis, reflecting acute disease. There were focally extensive areas of neuropil malacia surrounding the necrotic neurons. In some areas of the cerebral cortex, more chronic lesions were present, with perivascular histiocytosis, endothelial cell proliferation and satellitosis of dead neurons by multiple glial cells. The neuronal necrosis in the cerebral cortex, thalamus and hippocampus confirmed the presumptive diagnosis of PEM.

The second calf was depressed, ataxic and blind, with periodic episodes of head pressing. The rectal temperature was 102.4°F. Treatment consisted of intravenous thiamine administered at 6.8 mg/lb (15 mg/kg; 1125 mg in 500 ml 0.9% NaCl) daily for 3 days. Appetite, attitude and vision were markedly improved after 3 days of treatment. Following resolution of ataxia, the calf was discharged from the hospital.

The Food Animal Production Medicine Section was asked to investigate the cause of the recurring episodes of PEM on this farm. The history revealed that on November 20, 1999, which was four days prior to the initial onset of neurological problems, the pelleted feed formulation was changed to increase the level of crude protein in the ration to 18%. At that time, a different protein source and an ionophore were included in the diet. The attending clinician recommended that the farm stop feeding the complete pellet, or to dilute its potential toxic effect by adding hay to the diet until the feed could be analyzed. On December 20, 1999, 1 to 2 lb of hay was fed daily to each calf, in addition to the pelleted ration. After the ration was diluted by feeding added hay, no new neurological cases were observed. On December 27, 1999, the farmer began feeding the pellet that was fed prior to the neurologic problems. To date, no additional neurological cases have occurred.

Laboratory Data

A sample of the pelleted feed was submitted for wet chemistry analysis to determine its nutrient composition (Table 1).

The only remarkable finding was the high sulfur content (0.56%, dry matter basis). A second sample was obtained and analyzed by wet chemistry with similar results. According to the National Research Council, the recommended requirement for sulfur in dairy calves is 0.16% on a dry-matter basis, and the maximum tolerable limit is 0.40%.[11] Excessive dietary sulfur is a cause of PEM and was considered to be the cause of this outbreak. Total erythrocyte transketolase activity was not measured, however there was adequate fiber in the diet, no amprolium was fed, and there was no evidence of ruminal acidosis. The CSF sodium level was elevated in one calf (122 mmole/L), however we believe this was secondary to being recumbent since the calves in each barn were offered water twice daily. The possibility of lead poisoning was considered, but following the marked improvement in most calves following therapy, lead levels were not measured.

Table 1. Nutrient analysis of the pelleted calf ration.

Nutrient	% of ration (dry matter basis)	Recommended dietary levels
Crude protein	21.14	16% (min.)
ADF	20.74	16% (min.)
NDF	39.07	23% (min.)
Calcium	0.99	0.50% (min.)
Phosphorous	0.72	0.32% (min.)
Magnesium	0.39	0.16% (min.)
Potassium	1.23	0.65% (min.)
Sulfur	0.56	0.16% (min.)/ 0.40% (max.)

Discussion

Problems associated with low to moderate excess of sulfur are increasingly recognized. Sulfur and sulfates are of low toxicity, but are rapidly converted to sulfide and sulfite in the rumen. Absorbed sulfide is normally oxidized to sulfate in the blood, and is then distributed to extracellular fluid. Sulfate is recycled to the rumen via saliva or directly to the large intestine.[6] Hydrogen sulfide gas is a product of rumen microbial metabolism, and in high concentration can produce necrotic brain lesions. However, there is debate whether the amount of hydrogen sulfide gas produced in animals exposed to elevated dietary levels of sulfur is sufficient to cause these lesions. It is possible that the enzymes needed to oxidize the metabolites may be overloaded, leading to necrotic brain lesions.[12] Brain tissue is vulnerable to oxidative damage due to its high lipid content. Sulfite-derived radicals are thought to cause lipid peroxidation and damage to biological membranes,[12] culminating in the histologic signs of PEM seen at post-mortem.

Although the the cerebrocortical lesions of sulfate toxicity and thiamine-dependent encephalopathy are similar, findings indicate there is no measurable alteration in thiamine status in animals intoxicated with sulfur.[8] When dietary sulfate toxicosis PEM was experimentally induced, erythrocyte transketolase activity and thiamine concentrations of the liver, brain, and

CSF were normal or high.[5] However, animals exposed to excess dietary sulfur and supplemented with thiamine are at considerably lower risk of developing clinical PEM.[4] Thiamine may act as a free radical scavenger and offer protection against sulfur's toxic metabolites produced in the rumen.[12]

Excessive intake of sulfur is primarily related to the concentration of sulfur in the feed, water or both. Assessment of the contribution of water to sulfur intake is made by estimating daily water intake, converting the sulfate to sulfur, and equating grams of sulfur consumed in the water to the estimated total daily dry matter intake.[7] Consumption of water containing a moderately high level of 1000 ppm of sulfates can contribute 0.10 to 0.27% of dietary sulfur intake. Significant uptake of sulfur by plants in areas with high levels of sulfur in the soil and water is common. Examples of feedstuffs commonly fed to dairy cattle containing high levels of sulfur are shown in Table 2.

In this case report, the origin of the elevated levels of sulfur in the pelleted feed was never determined. Actual scale weights for the custom pellet matched the mix specifications. The feed company provided the list of individual ingredients in the pellet, and we calculated the sulfur content of the ration to be 0.38%. This is higher than required, but still below the maximum tolerable level. Other potential sources of supplemental sulfur, such as Dynamate® (K_2SO_4 and $MgSO_4$), ammonium sulfate [$(NH_4)_2SO_4$], or gypsum ($CaSO_4$), were not found. Additionally, other constituents of these supplements, such as calcium or magnesium, were not elevated. The protein supplement (Table 3) included in the calf pellets just prior to the outbreak of PEM contained more sulfur than most protein sources, however a 10-fold error in either its inclusion rate or its sulfur content would be necessary to produce the measured elevation seen here.

Some corn by-product feeds are known to contain unusually high amounts of sulfur; however, none of these ingredients were included in the pellet.

Although it was not measured in these calves, hydrogen sulfide levels in the rumen gas cap may be suggestive of high dietary sulfur. Hydrogen sulfide levels in normal ruminants have been reported to be less than 500 ppm, whereas in clinically affected animals the range has been reported to be 6,900-13,500 ppm.[10] The technique for sampling and determining the hydrogen sulfide level in the rumen gas cap has been described.[10]

Table 2. Feedstuffs commonly used in ruminant diets containing high concentrations of sulfur.[11]

Feedstuff	% sulfur content (DM)
Alfalfa	0.40
Extracted cotton seeds	0.34
Beet pulp	0.22
Corn gluten feed	0.23
Soybean meal	0.49
Molasses	0.40
Wheatgrass	0.47
Dehydrated whey	1.12
Dried brewers grains	0.32

Table 3. Analysis of the protein supplement.[1]

Dry matter	90.0%
NE (lactation)	2.01 mcal/kg 0.91 mcal/lb
Ether extract	3.70%
Crude protein	50.00%
CP equiv from NPN	28.20%
NPN	4.5%
Undegradable protein	55.00% of CP
Degradable protein	45.00% of CP
Soluble protein	30.00% of CP
Acid detergent diber	7.5%
Neutral detergent fiber	30.00%
Non-fiber carbohydrate	20.00%
Ash	6.00%
Calcium	0.18%
Chlorine	0.20%
Magnesium	0.43%
Phosphorous	1.2%
Sodium	1.50%
Sulfur	2.44%

Conclusions

Problems associated with excess dietary sulfur in ruminants are being more commonly recognized. Outbreaks of PEM can result from excess dietary sulfur, as well as lead toxicosis, water deprivation or salt toxicity. High concentrations of hydrogen sulfide in the rumen gas cap provides evidence for excessive total sulfur intake, and suggests possible problems with feed and water sources. Prompt removal and sampling of suspect feeds for their sulfur content can also be a valuable diagnostic tool in outbreaks of neurologic disease in dairy calves.

Acknowledgements

Thank you to Dr. Jeffrey Bleck of Kettle Moraine Veterinary Center, S.C., Plymouth,WI for his assistance and referral of this case and Dr. Lynette Phillips for pathological assistance.

References

1. *Biovance Technical Services Bulletin*, Biovance Technologies, Inc, Omaha NE, 2000.
2. Divers TJ: Neurologic Diseases, in Howard JL, Smith RA (eds): *Current Veterinary Therapy 4: Food Animal Practice,* Philadelphia, WB Saunders Co, 1999, pp 660-661.
3. George LW: Diseases of the Nervous System, in Smith BP (ed): *Large Animal Internal Medicine.* St. Louis, CV Mosby Co. 1990, pp 943-948.
4. Gooneratne SR, Olkowski AA, Klemmer RG, *et al*: High sulfur related thiamine deficiency in cattle: a field study. *Can Vet J* 30:139-145, 1989.
5. Gould DH, Hamar DW, McAllister MM, Savage JC: High sulfide concentrations in rumen fluid associated with nutritionally induced polioencephalomalacia in calves. *Am J Vet Res* 52:1164-1169, 1991.
6. Gould DH: Polioencephalomalacia. *J Anim Sci* 36:309-314, 1998.
7. Hamlen H, Clark E, Janzen E: Polioencephalomalacia in cattle consuming water with elevated sodium sulfate levels: a herd investigation. *Can Vet J* 34:153-158, 1993.
8. Jeffrey M, Duff JP, Higgins RJ, *et al*: Polioencephalomalacia associated with the ingestion of ammonium sulphate by sheep and cattle. *Vet Rec* 134:343-348, 1994.
9. Jubb KV, Huxtable CR:The Nervous System, in Jubb KV (ed): *Pathology of Domestic Animals,* ed 4, Vol 1, San Diego, Academic Press, 1991, pp 340-343.
10. Loneragan GH, Gould DH, Callan RJ, Sigurdson CJ, Hamar DW: Association of excess sulfur intake and an increase in hydrogen sulfide concentrations in the ruminal gas cap of recently weaned beef calves with polioencephalomalacia. *J Am Vet Med Assoc* 213:1599-1604, 1998.
11. National Research Council. *Nutrient Requirements of Dairy Cattle,* ed 6. National Academy of Sciences, 1989.
12. Olkowski AA: Neurotoxicity and secondary metabolic problems associated with low to moderate levels of exposure to excess dietary sulphur in ruminants: a review. *Vet Human Toxicology* 39:355-359, 1997.
13. Rebhun WC: *Neurologic Diseases: Diseases of Dairy Cattle.* Media, PA, Williams and Wilkins Co, 1995, pp 415-417.
14. Rousseaux CG, Olkowski AA, Chauvet A, *et al*: Ovine polioencephalomalacia associated with dietary sulfur intake. *J Vet Med Assoc* 38:229-239, 1991.

Verocytotoxin-producing Escherichia coli 0157 on a farm open to the public: outbreak investigation and longitudinal bacteriological study

G. C. Pritchard, G. A. Willshaw, J. R. Bailey, T. Carson, T. Cheasty

Veterinary Record (2000) 147, 259-264

Verocytotoxin-producing *Escherichia coli* (VTEC) O157 phage type 2 (PT2) was isolated from three calves and two goats on a farm open to the public. Phenotypic and DNA-based typing showed that the strains were identical or very closely related to those obtained from an outbreak of VTEC 0157 infection in two separate family groups who visited the farm. No VTEC 0157 PT2 was isolated again from the farm during a 12-month longitudinal bacteriological study undertaken after the infected animals had been removed. However, phenotypically and genotypically indistinguishable VTEC 0157 PT21/28 strains were detected in two of 474 faecal samples collected at monthly visits from 15 species of animals of various ages. The two isolates were obtained from calves from different sources sampled 146 days apart, suggesting that the infection had persisted on the farm although it was not detected in the other species. The same strain was subsequently isolated from another calf housed in the same pen as one of the infected calves. The longest period during which the organism was excreted was seven days. No VTEC 0157 was isolated either from 204 replacement animals (including 138 orphan lambs and 10 calves) brought in from various sources, and sampled while they were kept in isolation for two weeks before being introduced to the farm, or from environmental samples. During the study a visitor became ill with VTEC 0157 PT2. However, the isolate was distinct from those recovered from the farm and there was no evidence to suggest that the visit was the source of the infection.