Case Report Rapport de cas

Ethylene glycol toxicosis in adult beef cattle fed contaminated feeds

Robert Barigye, Michelle Mostrom, Neil W. Dyer, Teresa K. Newell, Gregory P. Lardy

Abstract — Acute deaths of cows held in a drylot and fed several crop processing plant by-products were investigated. Clinical signs in affected cows included diarrhea, ataxia, recumbency, hypersalivation, and sunken eyes. A histological diagnosis of ethylene glycol toxicosis, based on numerous birefringent crystals in renal tubules, was supported by toxicologic findings.

Résumé — Empoisonnement à l'éthylène glycol de bovins de boucherie adultes nourris d'aliments contaminés. Une investigation a été menée à la suite de la mort subite de vaches gardées en enclos d'engraissement et nourries de divers sous-produits végétaux transformés. Les signes cliniques comprenaient de la diarrhée, de l'ataxie, du décubitus, de l'hypersalivation et des yeux enfoncés. Le diagnostic histologique d'empoisonnement à l'éthylène glycol, basé sur la présence de nombreux cristaux biréfringents dans les tubules rénaux, a été confirmé par les résultats toxicologiques.

(Traduit par Docteur André Blouin)

Can Vet J 2008;49:1018–1020

On October 10, 2006, an 8-year-old Angus cow (animal #1) and feed samples were received for necropsy and general investigation, respectively, at the Veterinary Diagnostic Laboratory (VDL) at North Dakota State University (NDSU). The case history indicated that 12 adult cross-bred beef cows had been found dead. The dead animals were part of a group of 130 head of cattle kept in a drylot. The herd was fed hay, beet tailings (a by-product of sugar beet processing), corn condensed distillers' solubles (CCDS), and 'molasses wash-out water' (MWOW) from a manufacturing plant that produced molasses-based lick tubs. A new batch of MWOW was fed on the previous Friday (designated Day 0) and the owner had not observed the herd over the weekend. On Monday (Day 3), he found 5 dead cows scattered over the drylot, and about 6 scouring, recumbent cows with sunken eyes. No treatment was administered to the affected cows, which eventually died. No other case was observed thereafter. Seven days after the 1st submission, an 8-year-old female Charolais (animal #2) was sent to the VDL for necropsy. This animal had developed the following clinical signs: ataxia, recumbency, hypersalivation, and death. Twenty-four days after the first deaths, the farm was visited to investigate the cause of the mortalities.

Department of Veterinary Diagnostic Services (Barigye, Mostrom, Dyer, Newell), and Department of Veterinary & Microbiological Sciences (Barigye, Dyer), North Dakota State University, 1523 Centennial Boulevard, Van Es Hall, Fargo, North Dakota 58105, USA; Department of Animal & Range Sciences, North Dakota State University, 100e Hultz Hall, Fargo, North Dakota 58105, USA (Lardy).

Address all correspondence to Dr. Robert Barigye, e-mail: Robert.barigye@ndsu.edu

Case description

Postmortem evaluation of animal #1 revealed frothy green ingesta extending from the oral cavity to the rumen. The rumen was severely distended and completely filled by this material. Apart from moderate epicardial ecchymoses, no other gross abnormalities were observed. These findings were consistent with a diagnosis of frothy bloat. The postmortem evaluation of animal #2 showed a markedly distended rumen that contained voluminous semiliquid ingesta. Using a pH strip, the rumen pH was determined to be about 7.0. In both submissions, representative tissue samples were taken from the lung, liver, kidney, spleen, heart, brain, adrenal gland, and small and large intestines, fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Five-micron sections were deparaffinized, stained with hematoxylin and eosin, and examined by light microscopy.

Histopathologic evaluation of kidney sections from animal #1 revealed rare foci of lymphocytic infiltration in isolated areas of the interstitium, and occasional mild necrodegenerative changes in some tubules. Evaluation of the sections under polarizing light showed rare birefringent crystals. Histopathologic findings in kidney sections of animal #2 were consistent with a mild interstitial nephritis, characterized by occasional foci of diffusely distributed lymphocytes. Multiple renal tubules contained abundant pink-staining intratubular casts, along with moderate to abundant crystalline material that was intensely birefringent under polarized light (Figure 1). Evaluation of the liver sections demonstrated a moderate, centrilobular to midzonal, lipidic degeneration of hepatocytes. A few rod-shaped bacteria, consistent with postmortem saprophyte proliferation, were also

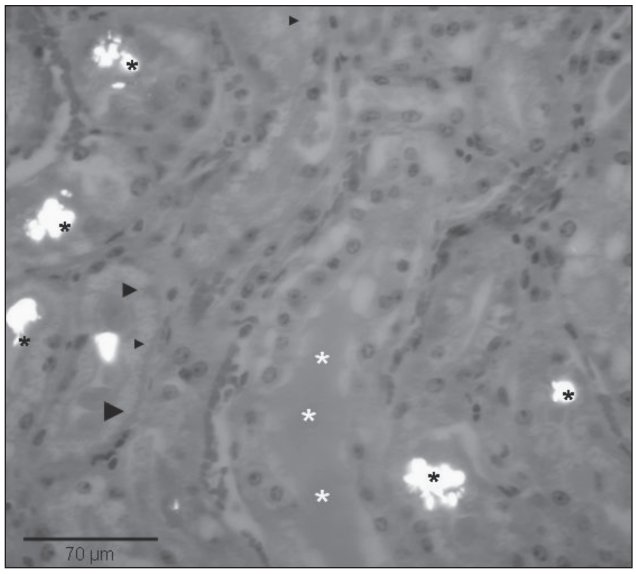

Figure 1. Bovine kidney – High-power photomicrograph showing numerous intratubular birefringent oxalate crystals (black asterisks), massive pink staining intratubular casts (white asterisks), and necrotic tubular epithelium (black arrowheads). Hematoxylin and eosin; polarizing light. Bar = 70 µm.

observed. A section of the spleen showed marked congestion and many hemosiderin-laden macrophages within the white pulp. A few intramyocardial *Sarcocystis* spp. cysts were seen in the heart. Morphologic diagnosis was acute tubular nephropathy with abundant birefringent crystals. Ethylene glycol toxicosis was considered the most probable cause. Ingestion of oxalogenic plants such as *Halogeton* spp., pigweed *(Amaranthus retroflexus)*, and greasewood *(Sarcobatus vermiculatus)* was considered in the differential diagnoses. Because there was no anamnestic indication of prior use of nephrotoxic antimicrobial agents like sulfonamides, the latter were not considered a possible differential diagnosis.

A field investigation was conducted on the affected farm to investigate the possible source of oxalogenic nephrotoxins. The beef herd was kept on a 100-acre drylot located several miles from the farm house. The drylot had been severely overgrazed, but no evidence of oxalogenic plants was identified. The drylot contained several abandoned vehicles, sheds, trees, and a water tank supplied by a shallow well. The sheds had been abandoned for some time and did not contain any stored chemicals. The vehicles appeared to be intact, and no leaks were observed on the ground. A water tank was located near the fence gate in a slough fed with spring-water further out in the pasture. The owner had been feeding hay from one source to the cows up until the time of mortalities. Eight cows from another location had also been fed the same hay throughout the summer and showed no clinical signs. Additionally, the cows in the drylot were fed sugar beet tailings, which had been left over since the spring. Corn condensed distillers' solubles were also offered free choice in open flat bottom wagons. The CCDS had been trucked to this property and to several neighboring farms from an ethanol plant. They were stored in an 18 920-liter (5000 gallon), above ground, storage tank on the farm. The owner had been feeding the CCDS and MWOW for the past 2 mo. He had been contracted to dispose of the MWOW on the soil, using his own truck and polyethylene tank, but an employee of the manufacturing plant had indicated that the by-product could be fed to cattle. The MWOW was fed in large plastic tubs. Shortly thereafter, the owner noticed that the MWOW appeared very "foamy;" particulary, the 4000-liter load (1000 gallon) given to the cattle on Day 0. Almost all of the MWOW was gone by Day 3. The producer also periodically fed the beef herd 'cull' molasses lick tubs. The latter were usually first off the production line and had not solidified. The herd had consumed 4 113-kg (250 lb) "cull" mineral lick tubs approximately 48 h prior to Day 0. Over the previous 2 mo, the producer had fed the cattle with over 20 "cull" molasses lick tubs.

No herd bulls or calves in the pasture showed clinical signs or died during this incident. The sugar beet tailings and hay had been fed for months to the cattle without any incident, and the CCDS was trucked to several neighboring cattle herds, none of which were experiencing cattle deaths. The owner expressed concern that the acute deaths were related to feeding the foamy MWOW offered to the cattle on Day 0. The majority of the sick and dead cows were observed on Day 3, and new cases were not seen thereafter. The owner stopped feeding the MWOW, sugar beet tailings, and CCDS following the deaths, and no more illness occurred. Samples of MWOW and CCDS, which had been submitted by the owner with animal #1, were tested for ethylene glycol (Texas Veterinary Medical Diagnostic Laboratory, Amarillo, Texas, USA). The samples were analyzed by gas chromatography with flame ionization detection. Results showed that the concentration of ethylene glycol in the MWOW and CCDS was 2% (20 922 mg/kg or ppm) and 22.4% (224 000 mg/kg), respectively.

Discussion

The diagnosis of oxalate nephropathy associated with ethylene glycol toxicosis as the cause was supported by the history and further corroborated by the analytical findings. Ingestion of oxalogenic plants was considered to be an unlikely differential diagnosis after failing to find any evidence of such plants on the affected farm. Moreover, *Halogeton* spp. and greasewood, both important oxalogenic plants, are not known to exist in southeastern North Dakota (1).

Ethylene glycol toxicosis is extremely rare in livestock but common in small animals (2). The most common sources of ethylene glycol toxicosis in North America are automotive antifreeze and windshield deicer fluids (3). However, this compound may also be found in many industrial solvents, detergents, corrosives, paints, and certain pharmaceuticals (4). Ethylene glycol or antifreeze toxicosis has been reported in a number of non-bovine vertebrates including cats (5) and dogs (6). The last publication on accidental ethylene glycol toxicosis-related cattle death in North America discussed an incident that occurred 28 y ago in a 1-month-old calf (7). Following this finding, an experiment conducted by Crowell et al (7) successfully reproduced characteristic lesions with doses of reagent or batch grade ethylene glycol (~99% to 100 % pure) in cattle at a dose of 2 to 10 mL/kg of body weight (BW). They reported preruminant

calves to be more susceptible than ruminating cattle. Clinical signs of intoxicated cattle included increased respiration, hypersalivation, ataxia, paraparesis, depression, recumbency, and death (7). These clinical signs are remarkably similar to those observed and reported by the owner in the present cases. Similar clinical signs were also reported in 4-to 5-month-old calves dosed with 12 mL of ethylene glycol/kg BW for 2 consecutive days, with death occurring in 3 to 5 d (8). Clinicopathological findings in the latter study were azotemia, hypocalcemia, neutrophilia, plasma hyperosmolality, and hemolytic anemia. Clinical signs in 4-to 5-month-old calves dosed at 7.5 mL/kg BW of ethylene glycol for 2 consecutive days were progressive depression and ataxia by 48 h postexposure; increased respiratory rate, transient lateral recumbency, hematuria, and abdominal pain by 5 d post-exposure; and anorexia and diarrhea on day 10 post-exposure (9). Most calves that survived returned to normalcy and started eating by day 20 post-exposure. Blood urea nitrogen and creatinine were significantly increased from day 2 to 10 post-exposure, and serum calcium was significantly reduced from day 1 to 10 post-exposure, suggesting that renal damage was occurring, related to calcium oxalate deposition in renal tubules and vasculature. No deaths occurred in these animals.

The lethal source of ethylene glycol in the present report was considered to be the CCDS, which contained 22.4% ethylene glycol, rather than the MWOW, which contained only 2% of ethylene glycol. Assuming a 500-kg (1100-lb) cow, which was typical in this herd, and a minimum lethal dose of ethylene glycol at 10 mL/kg BW (7), fatal poisoning of a single animal would require up to 5000 mL or 5 L of reagent grade ethylene glycol (~99% or 990 000 mg/L), which is approximately 4.95×10^6 mg of ethylene glycol. Mathematical calculations suggest that an individual cow would have had to consume at least 22.1 kg (48.6 lb) of CCDS for a lethal dose, which is an amount of CCDS that a cow might consume over 2 d given free choice access to the product. A plausible scenario to explain contamination of 2 feedstuffs from different sources was not found. The possibility of malicious poisoning was suggested as a possible cause, but to our knowledge, the owner did not pursue that investigation. No further clinical signs or deaths in cattle were reported after this incident.

Only 1 animal underwent necropsy after the initial death loss and that animal appeared to have died from bloat, although it did show a trace of renotubular oxalate crystals. Exposure to a high dose of ethylene glycol may have resulted in death prior to the development of marked renal oxalosis. This is possible, since only a small fraction of the ingested ethylene glycol results in calcium oxalate crystal formation (10). Our findings suggest that even though it is quite rare in cattle, ethylene glycol toxicosis should be considered as a differential diagnosis in acutely dying animals with renotubular oxalosis. These findings should also remind producers of the potential feed security issues that can be associated with the transportation, storage, and feeding of crop processing by-products.

Authors' contributions

Drs. Barigye, Dyer, and Newell carried out the histological evaluation of the tissue samples. Dr. Mostrom investigated the affected farm with Dr. Lardy and coordinated the field and laboratory investigations. Dr. Barigye wrote the manuscript in conjunction with the other authors. CVJ

References

1. Sedivec KK, Barker WT. Selected North Dakota and Minnesota Range Plants. Fargo, North Dakota: North Dakota State University Extension Service, 1997:EB–69.
2. Thrall MA, Grauer GF, Mero KN. Clinicopathologic findings in dogs and cats with ethylene glycol intoxication. J Am Vet Med Assoc 1984;184:37–41.
3. Jacobsen D, McMartin KE. Methanol and ethylene glycol poisonings. Mechanism of toxicity, clinical course, diagnosis and treatment [Review]. Med Toxicol 1986;1:309–334.
4. Kadiiska MB, Mason, RP. Ethylene glycol generates free radical metabolites in rats: an ESR in vivo spin trapping investigation. Chem Res Toxicol. 2000;13:1187–1191.
5. Beasley VR. Diagnosis and management of ethylene glycol (anti-freeze) poisoning, Feline Pract. 1985;15:41–46.
6. Khan SA, Schell MM, Trammel HL, Hansen SR, Knight MW. Ethylene glycol exposures managed by the ASPCA National Animal Poison Control Center from July 1995 to December 1997, Vet Hum Toxicol. 1999;41:403–406.
7. Crowell WA, Whitlock RH, Stout RC, Tyler DE. Ethylene glycol toxicosis in cattle. Cornell Vet 1979;69:272–279.
8. Singh DP, Kumar M, Varshney KC. Pathological changes in experimental ethylene glycol intoxication in cow calves. Indian J Animal Sci 1994;64:1361–1363.
9. Singh DP, Kumar M, Rao VDP. Experimental ethylene glycol toxicity in cow calves: Clinico-haematological and biochemical changes. Indian J Animal Med 1994;14:86–90.
10. Brent J. Current management of ethylene glycol poisoning. Drugs. 2001;61:979–988.