Lead arsenate poisoning in a herd of beef cattle

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- Old stores of lead arsenate, once a common insecticide used around orchards, may still exist on farms or ranches and are a hazard to livestock.
- Clinical signs of lead arsenate toxicosis often include rapid heart and respiratory rates; watery diarrhea, with or without blood; dehydration; and weakness.
- Diagnosis is based on clinical signs and appropriate heavy-metal analysis (arsenic and lead) of hepatic and renal tissue samples or urine samples.

One day after a herd of 91 crossbred heifers weighing approximately 230 kg each were moved from an area of poor grazing conditions to a winter wheat pasture with good forage availability, 1 heifer was found dead and 7 heifers staggered during ambulation. Those heifers were treated with thiamine by the rancher, without response. The remaining cattle were moved from the pasture to a dry lot. Five of the 7 heifers were dead the following day; the 2 remaining heifers with clinical signs were treated IV with calcium and magnesium solutions, and initially appeared to respond favorably. On the third day after the onset of clinical signs, 1 of the remaining heifers was found dead, and necropsy was performed. The other heifer was noticeably worse and was admitted to the teaching hospital for treatment.

On admission, the heifer had signs of depression, was dehydrated, and had hind limb hyperreflexia. Rectal temperature, heart rate, and respiratory rate were 38.9 C, 60 beats/min, and 24 breaths/min, respectively. Mucous membranes were pale, and capillary refill time was 3 seconds. Pupillary response was slow. The conjunctivae of both eyes were obviously congested. The medial canthi appeared to contain several drops of fresh blood, and bilateral mucous discharge and epiphora were evident. Feces were soft and mucoid, and had the odor of turpentine.

Blood biochemical analysis revealed acidosis (venous blood pH, 7.17; reference, 7.40), base deficit of 12.5 mEq/L, hypocalcemia (5.1 mg/dl; reference range, 8.5 to 11.5 mg/dl), uremia (BUN, 85 mg/dl, and creatinine, 13.5 mg/dl; reference range, 2 to 15 mg/dl and 1.1 to 2.1 mg/dl, respectively), and hypoglycemia (26 mg/dl; reference range, 46 to 82 mg/dl). Creatine kinase (6,976 IU/L; reference range, 19 to 75 IU/L), lactic dehydrogenase (2,540 IU/L; reference range, 176 to 365 IU/L), γ-glutamyltransferase (45 IU/L; reference range, 12 to 39 IU/L), and aspartate transaminase (393 IU/L; reference range, 87 to 217 IU/L) activities were high. Urinalysis revealed 3+ protein, too many renal epithelial cells to count, 14 to 20 casts/high-power field, and a strong reaction for occult blood.

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Treatment protocol on admission was based on history, clinical impressions, and venous blood gas values, and included IV fluid replacement with hypertonic sodium bicarbonate solution (2.5%) to correct half of the base deficit of 12.5 mEq/L. This was followed with IV administration of 20 L of 0.9% NaCl solution plus 10 mEq/L of potassium chloride at 1.5 L/h, to correct dehydration. Suspected hypocalcemia (on the basis of clinical signs and the referring veterinarian's comment that improvement was noticed following IV administration of calcium solution) was treated with 4.25 g of calcium gluconate, IV. Other treatments included thiamine (2.5 g, IV, and 2.5 g, IM); 120 mg of dexamethasone, IV; and 2.5 g of oxytetracycline, IV.

This heifer died the day after admission. At necropsy, edema in the intestinal mesentery and subserosa of the cecum and spiral colon was observed. Petechia and mild submucosal edema were observed in the abomasal mucosa. Ruminal and reticular contents consisted of roughage mixed with fluid. Abscesses filled with yellow semifluid pus were found in the cranioventral portion of the right cranial lung lobe. Substantial gross lesions were not evident in the heart, liver, or kidneys.

Microscopic renal lesions consisted of granular eosinophilic material in the tubules at the corticomedullary junction, without inflammatory cells. Intestinal and abomasal submucosae were edematous, and submucosal vessels were congested. The submucosa of the urinary bladder was mildly edematous. Notable microscopic lesions were not found in the brain, heart, or liver.

Arsenic and lead analyses were performed on hepatic and renal tissue samples obtained from the heifer that was dead on arrival and from the heifer that died in the teaching hospital. One gram each of liver and kidney tissues was digested in 10 ml of 1:1 nitric acid/deionized water for 4 hours. The digests were filtered and deionized water was added for a total volume of 10 ml for arsenic analysis and of 100 ml for lead analysis. Analyses were performed by atomic absorption spectrophotometry, with Zeeman correction.[a] Arsenic analysis also was performed on urine samples collected from the treated heifer. For both heifers, arsenic concentrations in liver (5.14 and 4.39 μg/g; reference range, 0.004 to 0.40 μg/g) and kidney (5.12 and 4.81 μg/g; reference range, 0.018 to 0.40 μg/g) tissue samples were considered diagnostic for arsenic poisoning. Arsenic concentration in the urine from the hospitalized heifer (10.7 μg/g; reference range, 0.09 to 3.0 μg/g) also was high and aided in confirmation of toxicosis. Lead concentrations in the liver samples (5.33 and 5.00 μg/g; reference range, 0.1 to 1.0 μg/g) also were diagnostic for lead poisoning.

Because of the high tissue concentrations of arsenic and lead, lead arsenate was suspected as the toxicant responsible for the deaths in this herd. Inspection of an open shed located in the pasture revealed an open sack containing lead arsenate. The cattle had had free access to the sack in the shed.

Lead arsenate was once a common insecticide used around orchards,[1-3] and has been used as an anticestodal compound in ruminants.[4] Lead arsenate has not been registered for use or sale in the United States since 1988,[5] but is still used in other countries as an orchard and garden insecticide.[6] Clinical signs of lead arsenate toxicosis often include rapid heart and respiratory rates; watery diarrhea, with or without blood; dehydration; and weakness.[1,7-9] These clinical signs relate more to arsenic than to lead toxicosis.[7-10] The clinical signs of arsenic toxicosis may be so acute that those of lead toxicosis are not detected.[7]

Lead arsenate is a salt of arsenic acid, and thus is a pentavalent arsenical. Pentavalent arsenicals are not as readily absorbed from the digestive tract as are the trivalent forms, and are easily excreted in feces. Once absorbed, pentavalent arsenic is readily excreted by the kidneys, whereas trivalent arsenic is more readily excreted into the intestine via bile.[11] Pentavalent inorganic arsenic is relatively stable at neutral or alkaline pH, but undergoes reduction with decreasing pH.[12] A small fraction of pentavalent arsenicals can be reduced to the trivalent form in the kidneys, which may cause nephrotoxicosis.[9]

Pentavalent arsenic may be reduced to arsenic trioxide in vivo. The biochemical mechanism for in vivo methylation of inorganic arsenic is a reductive process, and reduction of arsenic in vivo is presumed to relate to biomethylation.[13] Via in vitro techniques, isolated hepatocytes have been demonstrated to readily methylate trivalent arsenic, whereas methylation of pentavalent arsenic is virtually nil. This report suggests that pentavalent arsenic must first be converted to arsenite prior to methylation.[14] Arsenic is believed ultimately to exert most of its effects by reacting with sulfhydryl groups in cells. As a result, sulfhydryl enzyme systems essential to cellular metabolism are inhibited. Thus, the net effect is blocking of fat and carbohydrate metabolism and cellular respiration.[11]

Arsenic affects tissues that are rich in oxidative enzymes, including the liver, kidneys, and alimentary tract. Dilatation and loss of capillary integrity account for congestion and edema of the intestinal mucosa and loss of fluid into the intestinal lumen. Loss of intravascular fluids results in hypotension, shock, and circulatory collapse.[9]

The blood biochemical abnormalities and pathologic findings in the hospitalized heifer were consistent with the dehydration, acidosis, and shock that accompany arsenic poisoning. Severe dehydration resulted from fluid loss into the intestinal lumen because of the damaged mucosal lining. Acidosis is a common sequelae to loss of intravascular bicarbonate into the intestinal lumen, decreased renal function, and dehydration. Decreased circulating blood volume (from fluid loss) resulted in shock and eventual cardiovascular collapse. The hypoglycemia observed in this heifer could be explained by a 14-hour lag time between sample collection and analysis, with resultant consumption of glucose by RBC in the sample. Ocular lesions noticed on physical examination were attributed to loss of capillary integrity in conjunctival vessels and subsequent hemorrhage.

The key to successful treatment of acute inorganic arsenic poisoning is early diagnosis. Even so, treatment may be unrewarding. When toxicosis is diagnosed early, cattle should be treated with large doses of a saline purgative, in an attempt to remove the unabsorbed material from the gastrointestinal tract. Sodium thiosulfate has been recommended to be given PO and IV.[11] Activated charcoal is indicated after recent exposure, along with vigorous fluid and electrolyte therapy.[9] Dimercaprol is a sulfhydryl-containing antidote that is felt to be specific for trivalent arsenic; however, its value as a therapeutic agent for arsenic poisoning in large animals is questionable. If administered, it should be in a 5% mixture with a 10% solution of benzyl benzoate in arachis oil at a dosage of 3 mg/kg of body weight, IM.[15] Results in large animals may have been disappointing because veterinarians have not repeated the treatment every 4 hours for the first 2 days, every 6 hours on the third day, and every 12 hours for the next 10 days.[11] Lipoic acid[b] is a chelating agent that has been found to be superior to dimercaprol when administered as a 20% solution to calves exposed to arsenic.[9] Lipoic acid is administered at a dosage of 50 mg/kg, IM, at 2 to 3 injection sites every 8 hours.[15]

Meso-2,3-dimercaptosuccinic acid and 2,3-dimercapto-1-propanesulfonic acid, sodium salt are water-soluble analogues of dimercaprol that are less toxic, more water soluble, and effective when given orally.[9] Succimer (2,3-dimercaptosuccinic acid)[c] is the first oral treatment approved by the US Food and Drug Administration for lead poisoning in children.[16] It has an added benefit in that it also chelates other heavy metals, including arsenic and mercury, and has not been found to significantly increase excretion of iron, calcium, or magnesium.[16] Succimer has been studied in animals and adult human beings for at least 25 years. Many of these studies were performed in China, Japan, and the Soviet Union.[17] Wholesale cost to the pharmacy is approximately $300 for one hundred 100-mg capsules. This cost would correlate with approximately $800 to $1,500 to treat a 110-kg calf (extrapolating from the human dosage of 10 mg/kg, q 8 h, for 5 days; then 10 mg/kg, q 12 h, for 14 days). The cost prohibits the use of succimer in large animals at this time, but it may be useful in treating heavy-metal poisonings in small animals (approx $70 to $200 to treat a 15-kg dog).

[a]Perkin-Elmer 5000 Atomic Absorption Spectrophotometer, Perkin-Elmer Co, Norwalk, Conn.

[b]Sigma Chemical Co, St Louis, Mo.

[c]Chemet, McNeil Consumers Products Co, Fort Washington, Pa.

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Assessment of protection from systemic infection or disease afforded by low to intermediate titers of passively acquired neutralizing antibody against bovine diarrhea virus in calves

After establishment of a range of passively acquired viral neutralizing titers in colostrum-deprived calves by feeding of milk replacer, challenge exposure with virulent noncytopathic bovine viral diarrhea virus was performed. Calves were evaluated for fever, leukopenia, thrombocytopenia, and diarrhea; viral isolation and titration were performed on nasal secretion, buffy coat cells, and serum specimens. Calves with viral neutralizing titer lower than 16 developed severe clinical disease and manifested all of the aforementioned clinical signs. Fever and systemic spread of virus were detected in calves with neutralizing titer between 16 and 256. Severity of signs decreased as antibody titer increased. Thus, low to intermediate titer of passively acquired neutralizing antibodies to the virus were not sufficient to fully protect calves from virulent bovine viral diarrhea virus.—*Steven R. Bolin, Julia F. Ridpath in Am J Vet Res 56 (June 1995).*