PEER REVIEWED

Ergot toxicosis causing death in weaned beef calves

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Abstract

Eight bull beef calves weighing approximately 500 lb (227 kg) died following consumption of toxic levels of ergot alkaloids during the summer of 2012. Survivors demonstrated chronic effects of ergot alkaloid toxicosis, including poor growth and hyperthermia. All 60 calves on the farm had been weaned for 3 weeks at the time of the incident, and were consuming a free-choice pelleted creep feed which was identified as the source of the toxin. Two common sources of ergot alkaloid in livestock in the United States are tall fescue grass infected by the fungal endophyte *Neotyphodium coenophialum*, and *Claviceps purpurea*-associated sclerotia on seed heads of grasses or cereal grains. Toxic levels of ergot alkaloids in commercial feed as found in this case is not common.

Key words: ergot, endophyte, fescue, *Claviceps*, *Neotyphodium*

Résumé

Huit veaux de boucherie mâles pesant approximativement 500 lb (227 kg) sont morts suite à la consommation d'alcaloïdes de l'ergot à des concentrations toxiques durant l'été de 2012. Les survivants montraient des effets chroniques de la toxicose associée aux alcaloïdes de l'ergot incluant une faible croissance et l'hyperthermie. Tous les 60 veaux de la ferme avaient été sevrés depuis trois semaines au moment de l'incident et consommaient à volonté de la moulée de démarrage granulée identifiée comme étant la source de la toxine. La fétuque élevée infectée par l'endophyte fongique *Neotyphodium coenophialum* et les sclérotes associées à *Claviceps purpurea* sur les têtes de semence des graminées ou des céréales à grains sont deux sources communes d'alcaloïdes de l'ergot chez les bovins des États-Unis. On retrouve rarement des concentrations toxiques d'alcaloïdes de l'ergot dans la moulée commerciale comme ce fut le cas ici.

Introduction

Ergot alkaloids are mycotoxins produced by fungi and endophytes known to adversely affect humans and animals. In cases of significant or prolonged exposure, adverse effects can be severe and can cause death. Ergot alkaloid exposure in livestock is generally associated with ingestion of contaminated feed. Two common sources in the United States include tall fescue grass infected by the fungal endophyte *Neotyphodium coenophialum*, and *Claviceps purpurea*-associated sclerotia on seed heads of grasses (ryegrass and brome grass) or cereal grains (e.g., barley, wheat, and oats). A wet, cool spring followed by hot and humid weather can promote more fungal development of *Claviceps purpurea*. Pastures grazed or used for hay can be contaminated with both types of fungus, and ingestion of ergot alkaloids can cause a wide range of clinical signs. When the environmental temperature and humidity are high, ergot alkaloids induce vasoconstriction, hyperthermia, and in some cases bronchoconstriction. Clinical signs associated with ergot alkaloid exposure include depression, hyperthermia, open-mouth breathing, reproductive effects such as poor conception and abortion, and anorexia. Prolactin secretion from the anterior pituitary gland can be inhibited by ergot alkaloids, resulting in poor milk production and poor weight gain for calves nursing cows. In cold weather, vasoconstriction can result in loss of ears, tails, or even feet (fescue foot) due to tissue anoxia; in some cases frostbite can occur. In isolated cases, ergot alkaloid-associated capillary endothelial damage can result in hemorrhagic discharge from the nares or rectum. The treatment of choice includes removal of feeds containing ergot alkaloids, reducing stress, and good supportive care. Fescue pastures that contain endophyte-infected tall fescue can be reseeded or interseeded with other forages.

Case Report

A group of 60 registered Red Angus beef calves weaned 3 weeks earlier became ill on a central Iowa farm during the dry, hot summer of 2012. A field investigation was initiated after multiple calves died in a short period of time. The calves weighed approximately 500 lb (227 kg), and had been in good health, according to the owner. Calves had free-choice access to grass hay along with a free-choice commercial pelleted creep feed in a free-flowing, gravity-fed feeder. The ambient temperature through the several days of the disease period reached 100°F (37.7°C) and above. No abnormalities were observed in cows penned adjacent to the calves, and yearling heifers in another yard in close proximity were normal.

Upon arrival at the farm, 4 calves were dead (1 died 24 hours prior, and 3 died closer to our arrival) and 5 recumbent calves were in the barn yard. Two of these calves died acutely during examination and prior to initiation of treatment. The 3 remaining calves had rectal temperatures of 111°F, 110.5°F, and 109.5°F (43.9°, 42.6°, and 42.1°C). These calves were depressed, had decreased respiratory rates (25/min), ataxic, and were slow to stand. The calf with the highest rectal temperature was unable to stand. The calves were cooled by water from a hydrant.

All of the severely affected calves (recumbent or dead) were bulls. Other calves, including heifers, had clinical signs indicative of hyperthermia, with open-mouth breathing, rapid respiration rate, lowered head, and depression. Several calves had slight hemorrhagic discharge from the nares, some with bloody rectal discharge, and several were hypersalivating.

A field postmortem examination was performed on 3 calves. Gross examination of the lungs did not reveal evidence of pathology associated with acute bacterial or viral pneumonia. Petechial hemorrhages were present in the lung and trachea, and severe hemorrhage on the endocardial surface that continued through the myocardium of the left ventricle in all calves examined postmortem. Gross examination of other body systems was unremarkable. Tissues collected from field necropsies and feed collected from the pen were submitted to the Iowa State University Veterinary Diagnostic Laboratory. In addition, the last 2 calves that died during examination were submitted to the pathologist for full necropsy. The feed samples included commercial feed samples from the feeder as well as hay samples.

The owner of the calves stated he had used the pelleted creep feed for the previous 5 years as a post-weaning diet. The creep feed contained forage and roughage products (<70% dry matter) as well as processed grain by-products and grain products. The feed also contained chlortetracycline (140g/ton) and lasalocid (68g/ton). The feed label reported it contained 14% crude protein, 1% fat, and 25% fiber with a balance of minerals and vitamins. There was no evidence of rumen acidosis or acute grain overload in the calves, such as lowered rumen pH or evidence of gray, loose, foamy stools.

The producer was advised to remove the commercial pelleted creep feed from the calves as it was possible that the feed was the cause of the clinical signs observed. The owner removed the feed immediately. A large round bale consisting of grass hay was being fed in a bale feeder in the pen and was left for feed. Cows and heifers located in adjacent pens were also being fed hay from the same source. The pen where the calves were housed had a shaded barn area and adequate space.

The calf with the 111°F (43.9°C) rectal temperature remained recumbent and died the next day. This calf was also submitted to the state diagnostic laboratory. In total, 8 bull calves died. The surviving calves were moved to a shaded hoop building and survived, although they showed clinical signs of hyperthermia over the following 3 to 4 weeks as the ambient temperature remained in the plus 90°F (32°C) range. The calves were sprayed with water the following 4 weeks when afternoon ambient temperatures increased. No more deaths occurred after calves were moved to the shaded hoop barn. Because of poor weight gain and the possibility of chronic poor health, the calves were sold the following March as feeder cattle rather than breeding animals.

Diagnostic Laboratory Findings

A consistent gross finding in all necropsied calves was extensive endocardial and full-thickness myocardial hemorrhage in the left ventricle. There were no remarkable pathologic findings in the digestive or respiratory systems. Myocardial tissue from all calves examined microscopically had focal areas of widespread endocardial and full-thickness myocardial hemorrhage in the left ventricle. One calf had focal myocardial degeneration and loss of striation of the myocardium. Another calf also had a focal area of laminar necrosis in the cerebrum, in addition to the heart lesions. These findings are consistent with previous studies of heat stroke.[4,5,17,18]

There was no significant bacterial growth from tissues submitted for culture. Fluorescent antibody examination for clostridial organisms was negative. Polymerase chain reaction testing of lung tissue for infectious bovine rhinotracheitis virus was negative.

Creep-feed pellets fed to the calves were analyzed for ergopeptide concentration. The pellets contained 300 ppb ergotamine, 95 ppb ergosine, 60 ppb ergocornine, and 40 ppb ergovaline, for a total of 495 ppb total ergoalkaloids. There was no detectable ergovaline in the hay sample analyzed. Analysis of the pelleted feed sample showed no detectable clenbuterol, ractopamine,

zilpaterol, or melengesterol acetate; lasalocid was present in the feed at 12 ppm or 12 grams/ton.

Final Diagnosis

The final diagnosis in this case was hyperthermia due to ergotism and elevated ambient temperatures. Rectal temperature in calves examined ranged from 109.5° to 111°F (43.1° to 43.9°C). Consumption of the pelleted feed over a 3-week period prior to this episode increased daily, thereby increasing consumption of ergopeptine alkaloids to a level that contributed to hyperthermia. Concentrations as low as 2.27 ug ergopeptine alkaloids/lb (5 ug/kg) body weight/day have been reported to cause signs of hyperthermia in beef cattle.[1] In the present case, there was approximately 495 ppb or ug/kg of feed of total ergopeptine alkaloids. If a 500 lb (227 kg) calf consumed the pelleted feed at 3% of its body weight, daily feed consumption would be approximately 15 lb (6.8 kg). At this level of consumption, approximately 3375 ug of ergopeptides would be consumed each day (495 ppb X 6.8 kg feed). A 500 lb (227 kg) calf consuming 5ug of ergopeptine alkaloids/kg body weight would need to consume 1135 ug of the toxic material to have clinical signs of hyperthermia. In this case, calves potentially consumed 3375 ug of ergopeptides/day.

Discussion of Ergot Alkaloids

There are 3 main sources of ergopeptine toxicosis (mycotoxicosis) in livestock in the US. Tall fescue grass has a symbiotic fungal endophyte, *Neotyphodium coenophialum*, associated with it that improves growth of the plant, but does not produce gross visible signs of endophyte fungal growth. The endophyte can grow in leaves, stem, or seeds produced by the plant. It will then produce a variety of ergopeptine alkaloid toxins, but ergovaline is the predominate alkaloid. The term "fescue toxicosis" is used, but rather than the grass itself, toxicity is due to the symbiotic growth of the fungus in the fescue plant.[15]

The second source, often called ergotism, is from the fungus *Claviceps purpurea*. Unlike tall fescue endophyte, this fungus is grossly visible on the seed head and is termed sclerotia, and will completely replace the ovarian tissue of the infected cereal grain or grass.[11] Cereal grains, including wheat, rye, triticale, and barley, as well as a variety of grasses including the endophyte-free and endophyte-infected tall fescue, are commonly ergotized.[10] It is easy to see the purplish-white fungal sclerotia or dark ergot body on the seed head, or even in harvested cereal grain products.

A third source of ergopeptine alkaloids can cause nervous ergotism called "staggers". This is from the endophyte *Neotyphodium lolia* that produces a pyrrolizidine-type alkaloid (loline) in some strains of perennial ryegrass.[14]

Plants capable of fungal growths that cause ergot toxicosis have a widespread geographical distribution. The many types of grasses in pastures throughout the US that can be infected by *Claviceps purpurea* or *Neotyphodium coenophialum* can produce ergopeptine alkaloid toxins. Both fungal sources produce a large variety of ergot alkaloids, encompassing up to 80 different indole compounds.[8,11,12,13] The ergopeptine alkaloids are also called ergot alkaloids. The predominate ergopeptine alkaloid from the fescue is ergovaline; other ergopeptine alkaloids include ergotamine, ergocristine, ergosine, ergocornine, and ergocryptine, and their toxic effects and mechanisms of action are essentially identical to ergovaline.

Ergot alkaloids typically cause 3 different effects on animals. The effects can be dose-dependent as well as weather dependent, and the amount of ergopeptine alkaloids consumed can affect the types of clinical signs or pathology seen. Three effects are peripheral vasoconstriction, hyperthermia, and reproductive effects of ergotism. The pathophysiology of the ergopeptine alkaloids is peripheral vasoconstriction as well as causing hypoprolactinemia. Ergot alkaloids interact with dopaminergic neurotransmission to block prolactin.[12,13,16,22] Ergopeptine alkaloid-induced vasoconstriction is associated with D1-dopaminergic receptor inhibition and partial agonism of gamma 1-adrenergic and serotonin receptors. These alkaloids also induce bronchoconstriction and pulmonary vasoconstriction, which further compromise ruminants' ability to dissipate heat, especially during hot environmental conditions. Affected animals have a poor appetite and other indications of poor performance as part of the syndrome called fescue toxicosis or "summer slump".

Hypoprolactinemia occurs when ergopeptine alkaloids stimulate lactotropic D2-dopamine receptors in the anterior pituitary gland and inhibit prolactin secretion. Ergovaline functions as a dopamine D2 agonist and alters prolactin and several other hormones in the body. This effect reduces the ruminant dam's ability to produce milk for lactational feeding of calves or milk production for human dairy products. Prolactin is also involved in the endocrine regulation of other physiological processes, including lipid and carbohydrate metabolism, maintenance of electrolyte balance, immune function, and steroidogenesis.[12,13]

In ruminants, the vasoconstrictive effects and capillary endothelial damage of ergopeptine alkaloids, whether of endophytic fescue or ergot origin, generally predominate and cause what can be referred to as the gangrenous form of ergopeptine alkaloid toxicosis. The gangrenous form generally occurs in cold, winter environments. Vasoconstriction and capillary damage resul

in diminished blood flow to the extremities resulting in lameness, and eventually dry gangrene and the loss of extremities. The hyperthermic form occurs in heat-stress conditions, and develops because of the animal's impaired ability to thermoregulate and dissipate heat. During warm conditions, cattle, sheep, and horses develop "summer syndrome", characterized by increased rectal temperatures, lethargy, ill-thrift, failure to gain weight, and intolerance to ambient heat.[12,13,16,22] Summer syndrome may partly result from alterations of hormonal (plasma cortisol, triiodothyronine [T_3]) and vascular control of body temperature.[3,19] In both the gangrenous and hyperthermia forms of ergopeptine alkaloid intoxication, animal comfort, lameness, and stress, as well as effects of environmental temperature and reduced caloric intake, likely play a major role in the pathogenesis of any adverse reproductive effects. Fat necrosis or lipomatosis has been observed with chronic fescue toxicosis in a variety of ruminant species, and is associated with masses of necrotic fat in the abdominal or pelvic cavities. This can lead to dystocia during parturition.

Additional clinical signs of fescue toxicosis may be reproductive failure characterized by reduced lactation (agalactia), abortions, prolonged gestation, weak offspring, stillbirths, and thickened placenta (horses and cattle).[1,15,20,21] Ruminants of both genders may also have decreased fertility.[6,7,23] Ovarian follicular dynamics can be adversely affected by interactions involving the hyperthermic and/or the prolactin-inhibiting actions of these ergot alkaloids and thermal stress.[7,11,12,13] Bulls grazing endophyte-infected pastures were observed to have altered sperm motility parameters compared with bulls grazing non-infected pastures.[7,11] Recent studies have suggested that ergot alkaloids can effect embryo quality and subsequent embryonic development.[7,12,13,24]

Ergovaline is the primary ergopeptine alkaloid associated with endophyte (*Neotyphodium coenophialum*) infected tall fescue. When total dietary concentrations of ergopeptine alkaloids exceed 100 to 200 ppb, adverse effects on livestock performance are observed. Clinical signs associated with excessive exposure to ergot alkaloids are dependent on the species and the physiologic state of exposed animals, environmental conditions during the exposure period, activities of and interactions between the individual ergot alkaloids, and the level and duration of ergot alkaloid exposure. Endophyte-infected fescue and claviceps ergotism in livestock may cause ataxia, convulsions, lameness, dyspnea, diarrhea, and dry gangrene of the extremities similar to fescue foot, neonatal mortality, reduced lactation, poor weight gains, lowered production, and lowered feed intake.[2,9]

Understanding mechanisms responsible for decreased calving and growth rates, delayed onset of puberty, and impaired function of corpora lutea in heifers at puberty consuming endophyte-infected fescue is an emerging field in reproductive toxicology. The condition decreases overall productivity through a reduction in reproductive efficiency, reduced weight gain, and lowered milk production. Reproduction in cattle may be further compromised by winter coat retention, increased susceptibility to high environmental temperatures, and light intolerance. [12,13] Endocrine effects in heifers associated with infected tall fescue include reduced prolactin and melatonin secretions, and altered neurotransmitter metabolism in the hypothalamus, the pituitary, and pineal glands. These compounds reduce prolactin, increase body temperatures, and have powerful vasoconstrictive effects. Neurohormonal imbalances of prolactin and melatonin, with restricted blood flow to internal organs, may be the principal cause of aberrant reproduction, poor hormonal function, and poor growth and maturation in livestock consuming endophyte-infected tall fescue.

Plants commonly associated with ergot alkaloids include oats and wild oats-ergot sclerotia; brome grasses-ergot sclerotia; orchard grasses-ergot sclerotia; wild ryes-ergot sclerotia; barley-ergot sclerotia; tall fescue-endophyte and ergot sclerotia; rye grasses-endophyte and ergot sclerotia; timothy grasses-ergot sclerotia; rye-ergot sclerotia; and wheat-ergot sclerotia.[11] Plants with little to no risk of having ergot alkaloids include alfalfa, clovers, corn, johnson grass, pearl millet, sorghum sudan, and soybeans.[11]

Conclusions

Eight bull calves died on the farm after 3 weeks of exposure to pelleted creep feed containing elevated ergot alkaloid levels. There was poor weight gain in the remaining calves as a result of ergotism and hyperthermia. Ergot alkaloids can produce many effects by vasoconstriction of the vasculature, capillary endothelial damage, and bronchoconstriction in the lungs, as well as negative hormonal effects on cattle. The effects can be multifactorial, including hyperthermia, death, poor reproductive effects on males and females, decreased lactation with poor calf growth, and dry gangrene of extremities on the body that are typical in cold weather. These ergot alkaloids are produced by several ergot alkaloids typical of 2 sources. Fescue grasses can be infected by *Neotyphodium coenophialum* endophyte that is not visible grossly, but can be found in the stem, grass blades, and the seed heads; and *Claviceps purpurea*, which will form sclerotia that can be seen as a dark or purplish-white body that completely replaces the ovarian seed on the head of many grass plants, and are visible grossly. There are no effective drug treatments for the physiological effects of the ergot alkaloids, therefore the best response is achieved by removing animals from forages infected with ergot alkaloids and reducing stress.

Acknowledgement

The authors declare no conflict of interest.

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