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Lathyrus hirsutus (Caley Pea) Intoxication in a Herd of Horses

T.C. Holbrook, L.L. Gilliam, F.P. Stein, S.E. Morgan, A.L. Avery, A.W. Confer, and R.J. Panciera

Background: Caley Pea (*Lathyrus hirsutus*) is potentially toxic to horses, but large case series are not reported.

Objectives: To describe the clinical signs of horses intoxicated with *Lathyrus hirsutus* and speculate on the neuroanatomical lesion localization and pathogenesis based upon the observed clinical signs.

Animals: Twenty-two of 25 horses ranging in age from 6 to 34 months were affected. Five affected horses were presented to the OSUCHVS for evaluation and treatment after having been attended at the ranch by a local veterinarian (ALA). An additional horse that had been euthanized was also presented for necropsy.

Methods: A case series is presented. Diagnostic evaluation included: physical examination, complete blood count, serum biochemistry, CSF analysis, EMG, ERG, upper airway endoscopy, muscle biopsy, and serum vitamin E analysis. The grain ration consumed by the affected horses was analyzed for ionophores and cultured for fungi: the hay was examined for toxic plants.

Results: Bermuda grass hay consumed by the horses contained large quantities of mature *Lathyrus hirsutus*. Acute clinical signs conform to earlier descriptions of *Lathyrus hirsutus* intoxication in cattle. Residual neurologic signs were characterized by incoordination in the rhythmicity of multiple gaits. Evidence of mild neurogenic muscle atrophy was recognized in 1 of 5 horses biopsied.

Conclusions and Clinical Importance: Caley Pea intoxication may occur within days of seed pod consumption. The neurologic signs are unique and suggest involvement of the upper motor neuron system and regions of the spinal cord influencing voluntary motor movement. Drought conditions during plant growth may increase the risk of toxicosis.

Key words: Caley Pea; Lathyrism; Neurologic disease; Spasticity.

There are more than 150 species in the genus *Lathyrus*, approximately 40 of which occur in North America.[1] Many, but not all, species contain novel amino acids and nitriles that are either neurotoxic or osteotoxic.[1–3] Though the toxicants are present in vegetative parts of the plant, they are more concentrated in the seeds. Lathyrism in humans, attributed to the consumption of various species of Lathyrus flour, has been known for centuries.[4] Poisoning in domestic animals results from consumption of maturing plants and seed pods grazed in the field or consumed in harvested hay. There are a number of accounts of lathyrism in various animals in the 19th and early 20th centuries.[1,5] The more contemporary veterinary literature includes reports of disease in horses,[6,7] and cattle,[8,9] that consumed hay or forage contaminated with modest quantities of one or another *Lathyrus spp*. Spontaneous disease has been reported in many species; disease has been experimentally induced in sheep dogs, rabbits, rats, and mice.[1,5,10–12]

From the Department of Veterinary Clinical Sciences, Center for Veterinary Health Sciences, Oklahoma State University, (Holbrook, Gilliam, Stein); the Oklahoma Animal Disease Diagnostic Laboratory, Stillwater, OK (Morgan); the All Around Veterinary Services, Bells, TX (Avery); and the Department of Pathobiology, Center for Veterinary Health Sciences, Oklahoma State University, Stillwater, OK (Confer, Panciera).

Corresponding author: T.C. Holbrook, OSUCVHS, 1 Farm Rd. Stillwater, OK 74078; e-mail: todd.c.holbrook@okstate.edu.

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Abbreviations:

CSF	cerebrospinal fluid
DDSP	dorsal displacement of the soft palate
EMG	electromyography
ERG	electroretinography
LLH	left laryngeal hemiplegia
OSUCVHS	Oklahoma State University Center for Veterinary Health Sciences
SAG	surface antigen

Materials and Methods

Approximately, 60 horses on a single premise stationed in 3 lots according to age were at risk through access to a common forage source. Morbidity in Lot 1 (yearlings) was 21/25, in Lot 2, (2–3 year olds) 1/18, whereas 15 broodmares in Lot 3 remained free of related illness.

After an onsite assessment and treatment period of 2 weeks by one of us (ALA), 5 diseased and 1 euthanized animal were referred to OSUCVHS for diagnostic workup and treatment. Necropsy, comprehensive physical examination, complete blood count, serum biochemistries, serum vitamin E and selenium levels, cerebrospinal fluid analysis, EMG, ERG, upper airway endoscopy, and muscle biopsies were conducted. The grain was analyzed for ionophores and cultured for fungi. A specimen of hay was physically examined for toxic plants. The 5 horses were treated and returned to the ranch after 13 days of hospitalization. Finally, the ranch was visited (TCH, SEM, RJP), gaits of remaining affected horses were evaluated, and the hay bales that had been removed from each lot were examined to assess degree of contamination by *L. hirsutus*.

Results

Twenty-two horses in Lots 1 and 2 developed acute neurologic signs 4–7 days after the introduction of locally purchased hay and a new batch of grain ration. Affected horses were of similar Quarter Horse

breeding and ranged in age from 7 to 34 months. There did not appear to be a sex predilection as fillies, colts, and geldings were affected; however, the owner noted that those with more severe signs tended to be the smaller, younger horses (which tended to be the females). The older horse affected was a gelding that was considered to be the dominant horse in Lot 2, which contained 18 horses. Acute signs noted by the referring veterinarian included a reluctant, short-strided, stilted gait with the hind limbs placed further forward than normal, and the hind quarters dropped with the pelvis flexed. Some affected horses had firm epaxial and gluteal muscles without muscle tremors or sweating. An abnormal gait was noted in 21/25 of the younger horses (6–11 months of age) in Lot 1, and in 1 horse 34 months of age, in a separate pen holding 18 horses 2–4 years of age (Lot 2). Treatment of the acutely affected horses on the farm included oral dimethyl sulfoxide (1 g/kg) and flunixin meglumine (2.2 mg/kg IV for 4 days). Signs of upper respiratory infection that developed in several yearlings in Lot 1 during this period were treated with ceftiofur crystalline free acid (Excede)[a] (6.6 mg/kg) (IM) once and again 4 days later. In addition, aureomycin crumbles[b] were fed to all horses in Lot 1. Over the next 10 days, affected horses in Lot 1 appeared more lethargic and spent excessive time in recumbency. When standing, the fore and hind feet were often closer together underneath the body (camped under), with the head positioned well below withers height. One yearling developed severe diarrhea attributed to antibiotic treatment. Thirteen days after the onset of illness, that animal was euthanized, and was transported along with 5 live, affected horses (4 yearlings, and one 2-year old) to the OSUCVHS for evaluation and treatment.

Major lesions in the euthanized yearling included mild bilateral bronchopneumonia and severe, regionally extensive, acute necrotic small intestinal enteritis and infarction. Multiple histologic sections of brain and spinal cord stained with H & E and with luxol fast blue/cresyl violet failed to reveal morphologic evidence of neuronal or fiber degeneration. Although this animal had acute neurologic signs similar to other afflicted yearlings, enteric complications attributed to oral antibiotic treatment rather than lathyrism led to the decision for euthanasia.

During hospitalization, each of the 5 horses was generally lethargic, and 4 of the 5 youngest were moderately thin with body condition scores of 4/9. Three of the 5 stood with the head lower than withers height, often with all 4 limbs closer together underneath the body. Two horses had fine muscle fasciculations, one in the neck and shoulder after exercise, the other in the pectoral and gluteal regions after rising. Two horses frequently shifted weight in all 4 limbs, but worse behind. Evaluation with hoof testers was unremarkable, and the treading behavior was not altered by local anesthesia of the digital nerves.

Cranial nerve examination, tail and anal tone were normal in all horses. All had normal resistance to a static tail pull and normal strength and compensation during the dynamic tail pull. When the younger horses from Lot 1 were walked the gait was spastic; the stride length of all limbs was short and asymmetric, especially in the hind limbs. The coordination between limbs was inappropriate, both diagonally between contralateral fore and hind limbs, and horizontally between the forelimbs, hind limbs, or both. Some horses paced at a walk, and others appeared to lope on one lead in the front while walking behind. The gait deficits tended to worsen with increased exercise duration and speed. Several horses had a normal gait at a walk, and slow trot, but would transition to bunny-hopping at faster gaits. With increased speed, some individuals knuckled over at the fetlocks when cantering either briefly dragging both hind limbs, or holding 1 hind foot (sometimes alternating feet) up for several strides if only 1 limb was affected. The back appeared stiffened and the pelvic girdle was flexed forward with the hind quarters dropped. Proprioceptive deficits were not detected in any horse. The epaxial musculature appeared symmetrically atrophied in most of the young horses (Lot 1). Fundic examination, as well as ERG, did not reveal any abnormalities. Upper airway endoscopy revealed Grade 2 left laryngeal hemiplegia (LLH) in 1 of 5, and intermittent dorsal displacement of the soft palate (DDSP) in 2/5 of the affected horses.

Results of complete blood count and serum biochemistry were within reference ranges for all horses with the exception of mild neutrophilia in 4 horses, lymphocytosis in 1, and hyperglycemia in 1. The CSF analysis from each was within normal limits. Serum concentration of selenium was low in 3 horses, (0.06–0.15; ref. range 0.17–0.25 ppm), whereas the serum concentration of vitamin E was high in each of the 5 (352–444) (ref. range 100–300 μg/dL).

EMG performed via needle insertion in the gluteal, epaxial, triceps, and cervical musculature on the 5 horses from Lot 1 was unremarkable. Gluteal muscle biopsies from these horses were stained with H&E, PAS, Gomori's Trichrome, Amylase PAS, NADH, and Oil Red O. Muscle fiber sizes, shapes, and distribution were within normal limits. There was no evidence of muscle necrosis or regeneration, abnormal glycogen or lipid accumulation, and mitochondrial staining appeared normal. In addition, muscle biopsies of the sacrocaudalis were histologically normal in 4/5, whereas 1 had moderate anguloid atrophy and mild angular atrophy and mitochondrial aberrations consistent with vitamin E deficiency and early Equine Motor Neuron Disease (EMND).

Cultures of feed samples for saprophytes revealed multiple types of *Curvularia spp.*—*Alternaria spp.* & *Cephalosporium spp.* Grain samples were negative for ionophores. The originally submitted hay sample contained scattered seed pods identified as *Lathyrus hirsutus*.

The hospitalized horses were supplemented with vitamin E (20 IU/kg PO, q24h).[c] Vitamin E supplementation was prescribed for several weeks for all horses, and the hay source for the groups of horses remaining on the farm was changed to good quality alfalfa. The gaits of the initially affected 22 horses (Lot 1) markedly improved over 4 weeks; however, some deficits remained noticeable in 3 of the young horses when moving at a canter. One year later, these horses were reported to be normal by the owner and were being ridden under saddle.

Discussion

The onset of disease in all of these animals occurred within 1 week after introduction of new shipments of grain and hay into the diet, suggesting intoxication and further, that the feed recently introduced was the likely source of the toxin. Initially, the grain was thought to be the more likely source, but testing for ionophores failed to produce evidence of such contamination. A specimen of Bermuda grass hay submitted at referral contained very limited quantities of *Lathyrus hirsutus* See Figure S.1. It was not until a farm visit that the magnitude of contamination of the hay by wild peas was fully appreciated.

The hay was grown under drought conditions which should favor the growth of drought resistant legumes like Lathyrus species; there is also a relationship between drought stress and increased toxicity.[13] We speculate that the extreme drought conditions in Oklahoma during the season when this hay was produced may have played a role in this herd toxicosis See Figure S2. for a map of the geographic range of this plant in the United States. Various factors could have been responsible for differences in morbidity among these groups of horses. Age and or body weight may have played a role; the group of horses with the most affected individuals was much younger (7–14 months) and lighter. It is possible that these animals ingested a higher dose on a per kilogram body weight basis. Further, the degree of contamination with *L. hirsutus* varied among the individual bales; that fed the yearlings was much more heavily contaminated than the bales in other lots.

The reluctance to move and short stride not caused by laminitis, coupled with the apparent spasticity, normal muscle enzymes and lack of proprioceptive, and cranial nerve deficits suggested potential lesions involving the upper motor neuron system and regions of the spinal cord influencing voluntary motor movement. While laryngeal hemiplegia and signs of roaring are commonly reported diagnostic features of intoxication by *Lathyrus spp*. in horses, the significance of LLH and DDSP in our cases was equivocal.[1,5,7] Unfortunately, examination of the recurrent nerve was not included in the necropsy of the euthanized animal. This outbreak involving more than 20 diseased horses provided opportunity to observe an extensive range of acute and chronic signs associated with ingestion of *L. hirsutus*. Prominent among the residual signs were abnormalities of gait orchestration that were apparent in multiple animals noted in a variety of different gaits. Some animals paced or had uncoordinated stride lengths at a walk, whereas others only exhibited an abnormal gait at the trot or canter. Interestingly, although stringhalt is described as a frequent gait abnormality associated with lathyrism by others, it was not present in this large group of affected horses.[1] The onset of acute clinical signs in this group of horses within 4 days of initial ingestion of Caley Pea contaminated hay, and the subsequent resolution of signs over several weeks is also inconsistent with other reports of lathyrism in horses. Most of the previous descriptions in horses are associated with *L. sativus* and *L. cicera* consumption; clinical signs develop weeks to months after ingestion and often include upper airway dysfunction associated with laryngeal paralysis.[12]

Locomotion in vertebrates is controlled by spinal rhythm-generating networks referred to as central pattern generators (CPGs) located in the cervical and lumbar intumescence.[14,15] The coordination of gait is maintained by rhythmic cyclical excitation and inhibition of flexor and extensor muscles within and between limbs. Given that 22 horses exhibited clinical evidence of abnormal gait execution in 1 or more gaits including the walk, trot, pace, and canter without evidence of proprioceptive involvement, we postulate that central pattern generator dysfunction can account for many of the clinical signs noted in these in horses. Histologic examination of the spinal cord and brain of the single acute case that underwent necropsy failed to reveal morphologic lesions. Others have indicated histologic demonstration of lesions within the CPG associated with movement disorders in horses (shivers) has been exceedingly challenging (Stephanie Valberg, personal communication). Alternatively, dysfunction of the CPG could be because of receptor mediated effects of the toxin which may not result in morphologically demonstrable neuropathology, especially considering the clinical signs in this group of horses were acute in onset and improved over time.

One toxic amino acid previously identified in *L. hirsutus and L. odoratus* is ϒ-glutamyl-β-aminoproprionitrile (BAPN), a compound known to cause osteolathyrism in young growing rats.[16,17] However, our experience in horses and that previously reported by Burrows in cattle documents neurotoxic disease rather than bone abnormalities caused by *L. hirsutus*.[1,8] This may be a function of species and/or age susceptibility as well as duration of ingestion; clinical evidence of osteoporosis required long-term feeding (3–4 weeks) of *L. odoratus* to growing rats.[17] Multiple other unique nonprotein amino acids have been identified in Lathyrus species. Amino acid profiles are unique among different species of Lathyrus and used to classify the plants into 5 separate groups based on amino acid content. Chromatographic methodology indicates *L. hirsutus* has a very different amino acid composition compared to *L.*

sylvestris and *L latifolius*.[18] Sheep fed *Lathyrus sylvestris* develop neurologic disease and this legume contains the amino acid 2,4 diaminobutyric acid (DABA).[11,19] The clinical signs reported in sheep, and apparent pathogenesis appear quite different from those reported here in horses associated with *L. hirsutus*. Clinical signs in affected sheep are consistent with hyperammonemic encephalopathy; DABA is known to inhibit ornithine decarboxylase which is required for urea metabolism and blood ammonia concentrations are increased in affected animals.[20] The amino acid thought to be central to the pathogenesis of human neurolathyrism, most often associated with the consumption *of L. sativus*, is N- β- -oxalyl-L-α,β-diaminopropionic acid (ODAP).[13,21] Recent studies indicate that ODAP causes neurotoxicity via excitation of metabotropic glutamate receptors in the spinal cord resulting in intracellular calcium accumulation and oxidative stress.[22] Excitotoxic mechanisms could be responsible for the epaxial stiffness and spastic gait noted in the acutely affected horses of this report; furthermore, neurodegeneration associated with chronic excitotoxicity could result in epaxial muscle wasting. Interestingly, rhythmic synchronous activation of metabotropic glutamate sensitive receptors within the spinal cord is required for the orchestration of gait.[23] Based upon the unusual spectrum of gait abnormalities noted in this group of horses, we suspect that the toxin(s) of *L. hirsutus* responsible for neurologic signs target(s) components of the CPG. ODAP concentrations were undetectable in *L hirsutus* via methods that identify high concentrations of this neurolathyrogenic amino acid in *L. sativus*.[24] Whether another as yet undefined bioactive amino acid present in *L. hirsutus* is the cause of the neurologic syndrome reported here, and the specific pathogenesis of this neurotoxicosis in horses is a matter for further investigation.

Footnotes

[a] Excede, Zoetis, Florham Park, NJ
[b] Aureomycin Crumbles; Alpharma Animal Health, Bridgewater, NJ
[c] Natural E 5000; Med Vet Pharmaceuticals, Eden Prairie, MN

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Conflict of Interest Declaration: Authors disclose no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Fig S1. Caley Pea seed pods from the contaminated hay sample. (Oklahoma Animal Disease Diagnostic Lab, Toxicology Laboratory).

Fig S2. The green shaded areas represent the states in which Caley Pea can be found. http://plants.usda.gov/core/profile?symbol = LAHI2.