Multiple bovine abortions with evidence of fetal locoism from pre-clinically intoxicated dams

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Abstract

Chronic consumption of specific plant species from the genera Oxytropis, Astragalus, Ipomeoa, and Swainsonia, commonly known as locoweeds, is well known to induce locoism in grazing animals. Locoism in cattle is characterized by sensory deficits, ataxia, behavior changes, loss of condition, and failure to grow. The toxic principle swainsonine is rapidly absorbed and distributed through the bloodstream to multiple organs where it inhibits cellular lysosomal alpha-mannosidase and Golgi mannosidase II, leading to lysosomal dysfunction and disruption of glycoprotein processing. Excessive mannose-rich oligosaccharide accumulations cause cytoplasmic vacuolation and cellular dysfunction. In addition to neurologic disease, chronic consumption of locoweeds is known to induce abortion and embryonic death in neurologically affected dams. We describe multiple cases of bovine abortion associated with chronic locoweed ingestion in non-clinical dams from a herd in southeastern Colorado. Neurons from the cerebral cortex, brainstem, cerebellum, and renal tubular epithelial cells displayed the characteristic cytoplasmic vacuolation observed in adult cases of locoism in the aborted animals. Although chronic ingestion of locoweed is widely known to cause early gestation embryonic death, late-term hydrops amnii, and fetal fluid accumulation, locoweed-induced abortion should be considered as a differential diagnosis for cases of non-infectious abortion in grazing cattle, even in the absence of maternal clinical signs. These findings indicate that the bovine fetus may be more sensitive to the abortive effects of swainsonine than previously thought.

Key words: bovine, fetus, locoweed, abortion

Introduction

Chronic ingestion of toxic locoweeds over a course of several weeks can induce locoism in grazing production animals and wildlife. As many locoweeds are native plants that...
can dominate certain plant communities, locoweed-induced toxicity is common and has been considered the most significant poisonous plant problem for livestock producers in the western United States. Grazing animals often prefer locoweed species during the fall, winter, and early spring when other palatable forage sources are not readily available. Clinical locoism is characterized by neurologic deficits including ataxia, sensory deficits, and behavioral changes as well as failure to thrive and loss of condition. Ingestion of locoweed by pregnant dams is also associated with reproductive complications that include early embryonic death, abnormal developmental of placental cotyledons, delayed placentation, hydrops amnii, congenital fetal malformations, and abortion. Together, the potential effects of locoweed consumption on production animals have extremely significant ramifications for producers.

Species from the genera *Astragalus* and *Oxytropis* are flowering perennial plants that occupy many plant communities in western rangelands. Although there are greater than 350 plant species in the 2 genera, only 24 species have been documented to contain sufficient swainsonine, the toxic indolizidine alkaloid that induces locoism. The swainsonine-containing species of *Astragalus* and *Oxytropis* in North America maintain a symbiotic relationship with fungal endophytes, and the endophytic fungus is solely responsible for producing the toxic swainsonine. The toxin-producing endophyte is vertically passed from mother to daughter in the seed coat, and locoweed species with decreased levels of the endophyte produce minimal swainsonine. Swainsonine is water soluble, and once ingested, is rapidly absorbed through the gastrointestinal tract into circulation. Cells of multiple organs absorb swainsonine, and it inhibits the enzymes lysosomal alpha-mannosidase and Golgi alpha-mannosidase II, which are required for normal cellular function. Inhibition of lysosomal alpha-mannosidase leads to the accumulation of mannose-rich oligosaccharides within the lysosome, and aggregation of unprocessed mannose in lysosomes produces cytoplasmic swelling and vacuolation observed histologically. Golgi alpha-mannosidase II is essential for N-glycan processing, and the inhibition of this enzyme by swainsonine results in improper glycoprotein processing. The severity of clinical disease depends on the dose-dependent degree of accumulation and amount of cellular dysfunction induced. Many different cell types in both adult cattle and fetuses are susceptible, but cytoplasmic vacuolation due to mannose accumulation is most often histologically prominent in the neurons of the central nervous system and epithelial cells of multiple organs, such as the kidney and endocrine organs. Gross lesions are not typically observed in the central nervous system or other affected organ systems, but congestive heart failure can occur in adult cattle poisoned at high elevations.

**Case History**

A herd of cross-bred beef cattle on open pasture in south-eastern Colorado suffered multiple late-term abortions in early spring of 2017. No evidence of clinical disease was observed in the dams that aborted. Two aborted fetuses were submitted to the Rocky Ford branch of the Colorado State Veterinary Diagnostic Laboratory for necropsy and diagnostic testing. Both fetuses had fully developed hair coats and partially inflated lungs, indicating that they were near full term, and histopathology of the lung confirmed inflation of the alveoli, consistent with attempts to breathe. Routine screening tests for infectious and non-infectious causes of abortion were performed on both fetuses. Testing for bovine viral diarrhea virus (direct fluorescent antibody test), infectious bovine rhinotracheitis (direct fluorescent antibody test), and *Neospora caninum* (PCR) was negative, and aerobic and anaerobic bacterial cultures failed to grow any pathogenic bacteria. No testing for *Leptospira* sp was performed. The concentration of nitrate within the aqueous humor was 10ppm (normal <20 ppm). Histological analysis of fetal brains identified marked cytoplasmic swelling and vacuolation in neurons of the brainstem and cerebral cortex (Figure 1, A-D). Similar lesions were discovered in many tubular epithelial cells in the cortices of the kidneys (Figure 1, E, F). These lesions were not specific for an etiology, but highly suggestive of a lysosomal storage disorder, and locoweed poisoning was considered as the top differential diagnosis. Prior to 2017, the herd had a documented history of locoism.
and locoweed species had been tentatively identified on the
property previously.

Suspicious plant samples from the affected ranch were
collected and submitted to the USDA Poisonous Plant
Research Laboratory for identification. The specimens were
positively identified as Wooly locoweed (Astragalus mollisili-
mus). Wooly locoweed is native to the Colorado plateau, and is
well recognized as a swainsonine-producing species capable
of inducing locoism in cattle. Swainsonine concentrations
within some toxic species can vary between geographically
separated populations, and this is at least partially due to
variations in the amount and strain of swainsonine-producing
endophytes that infect locoweeds and other swainsonine
containing plants. Swainsonine was successfully isolated
from the suspect plants using a commercially available solid-
phase extraction column and quantified using LC-MS/MS as
described previously. The swainsonine concentration was
determined to be 0.3% of total mass, a concentration that
has been shown to poison livestock. As swainsonine crosses
the placental barrier and locoweed-induced fetal lesions have
been described, several attempts were made to identify and
quantify swainsonine from fetal fluids, liver, and lung. No
swainsonine was identified in tissues or fluids from either
fetus; maternal serum was not available for analysis. Affected
dams later developed neurological disease consistent with
locoism in the weeks following the abortions.

Discussion

To our knowledge, the 2 cases presented here are the
first to document late-term bovine abortion associated with
minimal or subclinical maternal locoweed-induced neuro-
logic disease. The affected cows did later develop clinical
locoism.

The detection of swainsonine within serum or tissue
from the dams and fetuses in this case would provide in-
creased evidence of causation. The half-life of swainsonine
in serum is relatively brief, approximately 20 hours, and
affected dams were constantly on pasture with locoweed
species. However, locoweed may have been ingested inter-
mittently. Due to the short serum half-life of swainsonine,
previous consumption of locoweed, even a few days prior
to abortion, could have resulted in fetal lesions without
detectable serum swainsonine. Ingestion of 0.2 mg/kg of
swainsonine/day by sheep for at least 14 days is sufficient
to induce histologic lesions in multiple organs, and with a
concentration of 0.3% swainsonine, a 1100 lb (500 kg) cow
would only need to consume 30 to 40 grams or several hand-
fuls of locoweed each day to reach a dose of approximately
0.2 mg/kg/day. Additionally, the consumption preferences
of animals on pasture could vary from day to day, and it is
unknown what quantities of locoweed were consumed at
different times. In multiple years prior to 2017, the herd
had a documented history of clinical signs associated with
locoism in the adult cattle, including abortions from dams
with neurological deficits. Lastly, the fact that the dams in
the herd developed clinical locoism in the weeks following
the abortions lends support towards locoweed consumption
as the presumptive cause of the abortions.

Swainsonine toxicosis represents a unique acquired
lysosomal mannosidosis, but inherited mannosidoses have
been documented in cattle as well. All cattle breeds are
considered susceptible to locoweed-induced alpha man-
nosidosis, but autosomal recessive alpha-mannosidosis is
documented only in Angus, Galloway, and Murray Grey cattle.
An autosomal recessive beta-mannosidosis is known to occur
in Salers cattle. In both of the inherited mannosidoses, there
is a mutation in the gene encoding either alpha or beta-man-
nosidase that results in functional mannosidase deficiency
and lysosomal mannose accumulation. In contrast, toxic levels
of swainsonine inhibit Golgi mannosidase II function. In both
the inherited and induced conditions, the unifying feature is
impaired glycoprotein processing that results in pathological
lysosomal accumulation of mannose. The neuronal lesions in
both the inherited and induced mannosidoses are histologi-
cally indistinguishable.

Clinical signs of locoism are most frequently observed
in adult grazing cattle, whereas the manifestations of auto-
osomal recessive mannosidoses are typically seen in calves only.
Calves born with inherited alpha-mannosidosis demonstrate
reduced growth and progressive ataxia, and most affected
calves die by 18 months of age. Calves born alive to dams
poisoned with swainsonine may demonstrate small size,
diminished growth, and behavioral abnormalities similar to
the inherited mannosidoses. The herd in this case did not
have genetics from cattle breeds affected by the inherited
mannosidoses, and this observation decreased suspicion of
inherited mannosidoses as a differential diagnosis. In the case
of the inherited mannosidoses, a population history of weak
calves with progressive neurologic disease would have been
expected within the herd. Although adult cattle in the herd
had developed clinical locoism in the past, no neurologic dis-
ease or other fetal abnormalities had been reported in calves.
The observation of locoism in adult cattle, including the later
development of clinical signs in the dams that aborted the
affected fetuses, strongly supports locoweed poisoning as
the cause of abortion and the histologic lesions in this case.

Locoweed species are not unique in their ability to
induce abortion in cattle. Other abortifacient plants in the
western United States include Ponderosa pine (Pinus pon-
derosa), broom snakeweed (Gutierrezia sarothrae), and
nitrate-containing plants grown in high nitrogen content soil,
but no other known plants associated with abortion induce
the characteristic neuronal lesions of locoweed poisoning.
Species of lupines (Genus Lupinus) grow throughout many of
the western states and can cause fetal defects when consumed
by pregnant dams. Maternal lupine ingestion during days
40 to 80 of gestation results in fetal musculoskeletal defects
including arthrogryposis, torticollis, and cranial abnormali-
A
lupine toxicosis, and lupine poisoning was not considered as a differential diagnosis in this case.

**Conclusion**

Although the clinical effects of locoweed consumption on the reproductive system and pregnancy are well documented, the abortions reported here indicate that the threshold required to induce abortion is potentially lower than previously thought. This report has implications for clinical veterinarians and diagnosticians that are regularly presented with cases of bovine abortion in regions where locoweed species are endemic. Although abortions caused by locoweed consumption are typically seen only in dams with clinical locoism, locoweed-induced abortion should be considered as a differential diagnosis for cases of non-infectious abortion in grazing cattle, even in the absence of maternal clinical signs.

**Endnotes**

“Strata-X-C polymeric strong cation exchange, Phenomenex, Torrance, CA

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**References**


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