Case Report
Suspected swainsonine poisoning in a Belgian horse
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Summary
The case of a horse with acute symptoms of excitement, exaggerated fright reactions and trembling is presented. In addition to these cerebral symptoms, mild cerebellar ataxia and a renal tubular lesion were diagnosed. Suspected swainsonine poisoning was confirmed by the presence of the toxin (154 ng/ml) in the serum sample taken immediately after admission. A good recovery was seen after fluid therapy with supplementation of potassium, a dopamine drip and administration of diazepam. The effects of the toxin, by inhibiting the lysosomal enzyme α-mannosidase and mimicking the genetic mannosidosis, are discussed.

Introduction
Swainsonine is a toxic indolizidine alkaloid especially present in species of the genera Astragalus and Oxytropis, collectively known as locoweeds. The most notable clinical symptom of intoxication in horses is a change in behaviour, often characterised by many cycles of excitement/depression.

This is the first known report of swainsonine poisoning in a horse in Europe.

Case details

History
A 20-year-old male horse was admitted to the Internal Medicine department of the Faculty of Veterinary Medicine of the University of Ghent with symptoms of abnormal behaviour since the previous evening. The horse competed formerly at an international jumping level but had been retired to recreational use a few months prior to presentation. The owners described the horse as being usually quiet to handle. It now showed episodes of trembling and fright reactions when touched, and when the horse was lunged a hypermetria of the right hindlimb was observed. The symptoms had worsened and the horse was referred for further examination.

Clinical findings
On admission, the horse's rectal temperature, and heart and respiratory rates were all within reference ranges. Only the respiration was mildly elevated. The sclera of the eye was light yellow. The horse was extremely stressed. Examination of the cranial nerves was normal, but the reaction of the head during the menace response was exaggerated. When touching the body, the horse contracted all muscles and jumped away. From time to time there was a sudden short shaking movement over the whole body. When examining the horse on the lunge, a stiff gait but no paresis was seen. Only a slight hypermetria of all 4 limbs was observed.

Electromyographic examination of the back and hindlimb muscles revealed no abnormal potentials indicating denervation or muscle pathology. Blood gas analysis revealed a metabolic alkalosis (pH: 7.45; bicarbonate: 31 mmol/l; base excess: 7.7 meq/l). Blood biochemistry showed a very mild elevation of urea (9.5 mmol/l; reference range [rr]: 4–8 mmol/l), creatine phosphokinase (527 mu/ml; rr 10–146 mu/ml) and a very mild decrease of potassium (3.3 mmol/l; rr 3.5–4 mmol/l). The value for creatinine was at the upper limit of the reference range (16 mg/l; rr 5–16 mg/l). Urinalysis indicated a high level of γ-glutamyltransferase (110 iu/l; rr <20 iu/l). Normal values for the fractional excretion of sodium, potassium, chloride, calcium and phosphorus were found.

The following morning serum levels of potassium had decreased to 2.9 mmol/l and urea had increased to 10.9 mmol/l. The serum creatinine concentration remained unchanged. Clinically the horse was very excited and was trembling all over its body. When approaching the horse very carefully, it reacted in a frightened manner and a mild intention tremor was observed. The ataxia and hypermetria were more severe.

An echographic examination of both kidneys did not reveal macroscopic structural abnormalities. Diazepam (0.05 mg/kg bwt i.v., 4 times a day) was given in an attempt
to calm the horse. Polyionic isotonic perfusions with extra potassium added were administered. Six hours after starting the perfusions the horse had not urinated and rectal palpation revealed a small bladder; oliguria was suspected and the administration of i.v. dopamine (3–7 µg/kg bwt/min i.v.), to increase the renal blood flow and glomerular filtration and tubular flow, was started. The dopamine drip was continued for 3 days until oliguria was converted to polyuria. After 2 days of perfusion, potassium and urea were both normalised and the administration of the polyionic isotonic fluid was discontinued on the fourth day. The horse seemed to be less stressed and showed only short episodes of excitement and longer periods of depression and the diazepam was discontinued. During the following days the serum values of the electrolytes and urea were checked. On the fifth day after ceasing the perfusions the potassium dropped to 2.8 mmol/l. Potassium chloride was again given i.v. until the serum potassium level was normalised. Clinically, the horse was calm but it still showed mild ataxia. Gamma-glutamyltransferase in the urine had decreased to 67 iu/l. On Day 7 after admission, a second needle electromyographic examination and a transcranial magnetic stimulation with evaluation of the magnetic motor evoked potentials were performed. Neither test revealed any abnormality. During the following days potassium levels stayed stable and the horse returned home. Four months after the beginning of the problem, γ-glutamyltransferase in a control urine sample had normalised (18.0 iu/l). Over this period all clinical signs progressively disappeared and the horse was ridden again. One year later, the horse was still completely normal.

When evaluating the symptoms, 2 distinct problems could be described. The abnormal behaviour together with the ataxia and hypermetria indicate a central neurological lesion (cerebrum and cerebellum) whereas the uraemia, potassium abnormality, the high urinary level of γ-glutamyltransferase and metabolic alkalosis indicate a renal tubular lesion. To exclude a brain tumour in this aged horse a CT scan of the brain was proposed, but the owner refused.

**Discussion**

A possible differential diagnosis of the neurological problems together with the renal abnormalities is an intoxication. However, no toxin described in our countries could explain the symptoms. From a review of the literature, intoxication by swainsonine, present in locoweeds, is reported to induce abnormality, the high urinary level of γ-glucosidase and metabolic alkalosis indicate a renal tubular lesion. To exclude a brain tumour in this aged horse a CT scan of the brain was proposed, but the owner refused.

**Discussion**

The serum sample of the horse taken on admission (about 12 h after the beginning of the symptoms) was tested by a competitive binding assay with jack bean α-mannosidase and was found positive for swainsonine (154 ng/ml). The half-life of swainsonine in the serum is 16–20 h (Stegelmeier et al. 1995a). This means that an animal suspected of loco weed poisoning must have a blood sample taken within 2 days of eating loco weed for swainsonine to be detected. Blood samples from the same horse were also examined for swainsonine one day, one week and 4 months later. When the last sample was taken the horse was again clinically normal. All 3 samples were below the detectable limits (<30 ng/ml).
While the presence of the swainsonine in the first serum sample, together with the typical neurological signs and the renal abnormalities, are very suspicious for ingestion of feed containing swainsonine, locoweed ingestion was never confirmed. The horse was fed by ensilated grass hay and spent a few hours a day on pasture. Plants of the genera Astragalus and Oxytropis are present in Belgium, although the available literature does not state whether these variants produce swainsonine. The possible introduction and spread of toxic adventive species into Belgium by the increasing rates of human travel has to be taken into consideration. The presence of these plants was not confirmed in the silage or pasture.

Usually it takes several weeks of grazing the plants to become intoxicated. The horse showed symptoms in February 2005. Temperature and moisture conditions are ideal in mild winters so that locoweeds may retain green leaves and are very palatable to eat, especially when grasses are depleted. Dried locoweed that can be present in the ensilated grass hay could also be the source of the intoxication. Another source of swainsonine intoxication is the production of the toxin by certain moulds that can be present in the ensiled hay, such as Rhizoctonia leguminicola and Metarhizium anisopliae (Croom et al. 1995; Sim and Perry 1997). According to the owner, no macroscopic signs of growth of moulds was seen in the ensilated hay. However, no mycological examination could be performed on the hay.

Horses are described as being more sensitive to locoism than cattle. Also sensitisation occurs, which means that once they have eaten the plant they are more sensitive to the toxic effects than prior to exposure. Habituation may be manifested by ingestion of all plant parts (Ralphs et al. 1990). This may include eating soil containing the roots of locoweed after other parts of the plants have been grazed.

Van Kampen and James (1972) reported that histological lesions already developed within 4 to 5 days after animals began consuming locoweed. Vacuolation was first seen in the proximal convoluted tubules of the kidney and urinary bladder with slightly later lesions identified in the pancreas, thyroid, spleen, lymph nodes and cerebellum. Toxicokinetic studies by Stegelmier et al. (1995b) found that these tissues also accumulate relatively high amounts of swainsonine.

Mild cases generally resolve in 1–2 weeks. The inhibition of α-mannosidase is relatively transient and quickly reversible once animals stop eating locoweed (Stegelmier et al. 1994). However, regeneration of affected neurons in the brain and spinal cord may not occur completely, making horses a potential liability to human safety if ridden (James and van Kampen 1971). Patients with chronic locoism with longstanding clinical signs generally do not recover completely and the owner has to watch closely for future aberrant behaviour since these horses are notorious for throwing a fit when stressed or put into confined quarters, such as horse trailers.

An effective treatment for swainsonine poisoning does not exist (Staley 1978). Animals will recover from locoism provided they are removed from the toxin before extensive cellular degeneration has occurred in the brain. Further consumption of locoweed should be prevented immediately, and every year thereafter because animals may retain a preference for the plants from year to year.

The most effective management strategy is to deny livestock access to locoweeds during critical periods when they are more palatable than the associated forage (the late autumn, winter and spring) (Ralphs and James 1999). Rotating cattle from pastures with locoweeds to those without can also be effective to prevent poisoning. Herbicides can control existing locoweed populations and provide ‘safe’ pastures for critical periods. However, locoweed seed in soil will germinate when environmental conditions are favourable. Repeated application of herbicides will be necessary to control locoweed re-emergence. The method of conditioned food aversion by associating the eating of the locoweeds with a distasteful experience (e.g. a bolus of lithium chloride) seemed also to be an effective management system in cattle and horses grazing on heavily infested pastures (Ralphs and Provenza 1999; Pfister et al. 2002).

To the authors’ knowledge, this is the first report of a swainsonine intoxication in a European horse. The reason for the difference in prevalence between the United States and Europe is unclear. However, as with other plants, such as Senecio jacobaea, an increase in described cases of poisoned horses is seen, probably partly due to environmental management whereby less herbicide is used. Also, such management factors as overgrazing of pastures can be predisposing. We can conclude that by finding the toxin in this Belgian horse we have to assume that swainsonine poisoning has to be included in the differential diagnosis of equine neurological diseases in Belgium and perhaps in the surrounding countries, especially when symptoms of ataxia, hypermetria, hyperaesthesia and muscle tremors are presented.

References


