ZOO ANIMALS

Boxelder tree (*Acer negundo)* intoxication in fallow deer (*Dama dama*) and Dutch Landrace goats (*Capra aegagrus hircus*)

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SUMMARY

Within 10 days of ingesting boxelder tree (*Acer negundo*) cuttings, seven fallow deer (*Dama dama*) died (n=2) or were euthanased (n=5) after showing signs of colic, anorexia and severe depression. Another fallow deer and two Dutch Landrace goats (*Capra aegagrus hircus*) simultaneously displayed colic signs but survived. Therapy included intramuscular flunixine meglumine. Postmortem investigation revealed subacute renal tubular necrosis and extensive lung oedema in all animals, and three deer had liver degeneration. The combination of clinical history and postmortem findings lead to the presumptive diagnosis of maple leaf intoxication as described in equids. This is the first report of likely boxelder tree (*A negundo*) intoxication in animals and the first report of maple leaf intoxication in fallow deer and goats.

BACKGROUND

In horses (*Equus caballus*), maple (*Acer* species) ingestion may induce two separate intoxications. First, ingestion of small amounts of red maple (*A rubrum*) leaves results in an often fatal intoxication characterised by methaemoglobinaemia, Heinz body formation and haemolytic anaemia.[1 2] Second, consumption of boxelder tree (*A negundo*) and sycamore maple (*A pseudoplatanus*) seeds may inflict seasonal pasture myopathy (SPM)/atypical myopathy (AM) associated with hypoglycin A intoxication.[3 4] This results in acquired skeletal muscle multiple acyl-CoA dehydrogenase deficiency (MADD) with severe rhabdomyolysis.[4]

The causative toxins of red maples have not been completely characterised, but include gallic acid and a maple-specific potential co-oxidant.[5] At present, no clinical test is available to confirm the presence of toxin in suspected maple leaf intoxication cases. In MADD, specific toxic hypoglycin metabolites accumulate in the urine and serum.[6]

Diagnosis of maple leaf intoxication is based on the combination of clinical signs, history of maple leaf ingestion, clinical chemistry and postmortem investigation.[2]

Maple leaf intoxication was reported in grevy's zebra (*Equus grevyi*) and only once in non-equids.[7 8]

CASE PRESENTATION

To provide the animals browse, a herd of (1-10-7) fallow deer (*Dama dama*) and another herd (1-8) adult Dutch Landrace goats (*Capra aegagrus hircus*) were fed freshly harvested boxelder tree (*A negundo*) cuttings originating from another location in the park, consisting of branches, leaves and seeds. Their basic diet consisted of pellets (Tropische grazer brok, van Gorp Diervoeders B.V. Waalwijk, the Netherlands) and ad libitum hay. That day, one goat (#1, Table 1) displayed colic signs, and one fallow deer (#2) became recumbent. The following day, a second goat (#3) showed mild colic signs and anorexia. These three animals recovered.

In the following week, six other fallow deer (#4–#10) showed similar signs as colic, anorexia, hypothermia, shivering, increased respiratory rate and severe depression, were unresponsive to treatment and died spontaneously (#4, #5) or had to be euthanased without therapeutic intervention (#6–#10).

INVESTIGATIONS

Blood and urine samples from the second goat (#3) were submitted to Vet Med Labor (Ludwigsburg, Germany). Before euthanasia, blood samples were taken from deer cases 8–10. All blood samples had strongly elevated blood urea nitrogen levels (BUN) ranging from 23.3 to 71 mmol/ l (reference range: 3.5–7.1 mmol/l).

A urine sample of case 5 was collected immediately after euthanasia. Toxic hypoglycin metabolites were not detected.

All seven deceased fallow deer were submitted for necropsy. All showed severe lung oedema and renal pallor. One deer had severely oedematous muscles. All affected organs were sampled, routinely formalin fixed and processed to haematoxylin and eosin (HE) slides. Microscopic lesions (Table 1) consisted of severe lung oedema and extensive renal tubular necrosis with expansion of tubular lumina by proteinaceous fluid, intratubular haemorrhages and focal epithelial regeneration (Fig 1), in two deer (#6, #7) associated with haemolysis.

Bacteriological culture of intestinal contents from two deer (#7 and #10) revealed a normal intestinal flora.

Elevated BUN and creatinine values (in three deer and one goat) and the extensive renal tubular necrosis in all deceased animals indicated severe renal failure.

DIFFERENTIAL DIAGNOSIS

On admission of the deer for necropsy, the differential diagnosis included maple intoxication, tannin

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TABLE 1: Overview of affected animals and additional tests

	Animal				Lesions			Additional testing			
Case no.	Species	Age	Sex	Outcome	Kidney	Lung	Liver	Culture	Blood	Urine	Urine, hypoglycin
1	goat	adult	f	survived	–	–	–	–	x	x	x
2	fallow deer	adult	f	survived	–	–	–	–	x	x	x
3	goat	adult	f	survived	–	–	–	–	yes	yes	x
4	fallow deer	6y 2 m	f	died	acute tubular necrosis	oedema	degeneration	x	x	x	x
5	fallow deer	7y 2 m	f	died	acute tubular necrosis	oedema	iron storage	x	x	x	yes
6	fallow deer	3m	f	euthanased	acute tubular necrosis, haemolysis	oedema	degeneration	x	x	x	x
7	fallow deer	3m	f	euthanased	acute tubular necrosis, haemolysis	oedema	degeneration	yes	x	x	x
8	fallow deer	3m	m	euthanased	acute tubular necrosis	oedema	no degeneration	x	yes	x	x
9	fallow deer	3m	f	euthanased	acute tubular necrosis	oedema	no degeneration	x	yes	x	x
10	fallow deer	3m	f	euthanased	acute tubular necrosis	oedema	no degeneration	yes	yes	x	x

No., number; y, year; m, months; f, female; m, male; x, not done; –, not applicable.

intoxication, *Clostridium perfringens* infection and malignant catarrhal fever (MCF), urea toxicity from feed and other toxins. Tannin intoxication was ruled out by the absence of acorns in the intestinal tract or other associated lesions such as ulceration of the intestinal tract. Gross pathological, histopathological and bacteriological examinations excluded *C perfringens* infection in the fallow deer and systemic vasculitis, consistent with MCF, was absent. Other intoxications were considered unlikely, as apart from exposure to boxelder tree (maple) browse, diet was unaltered and remaining animals stayed healthy on the same diet. Finally, combination of extensive renal failure with the history of recent maple (boxelder tree) ingestion, lead to the presumptive diagnosis of maple leaf intoxication.

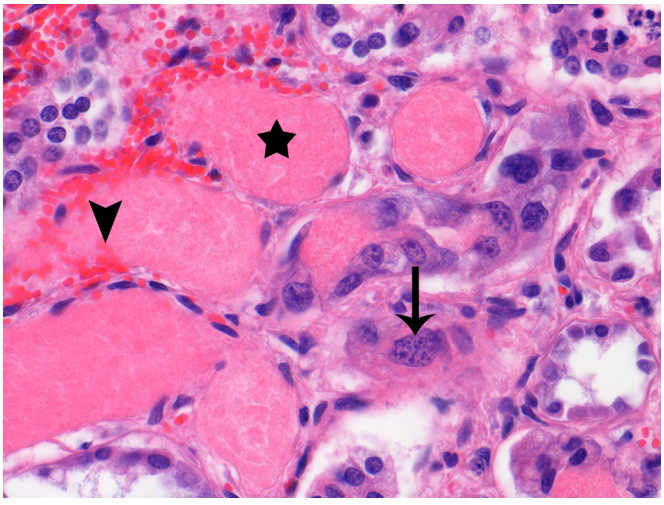

FIG 1: Subacute tubular necrosis, kidney, fallow deer case no. 6. Intratubular haemorrhages (arrow head), dilation of tubular lumen by proteinaceous fluid (asterisk) and necrotic tubular epithelium: the epithelial lining of dilated tubules (asterisk) is absent. Focal epithelial regeneration (arrow) indicated by large tubular epithelial cell with large nucleus. Haematoxylin and eosin (HE) staining, original magnification x 400.

TREATMENT

The first day, boxelder tree cuttings were removed, animals never had access to the tree. The first patients (#1–#5) were treated for colic signs with flunixine meglumine intramuscular (1.1 mg/kg body weight, Fynadine, Intervet, Boxmeer, the Netherlands). Cases #6–#10 presented in a very bad condition and had to be euthanised without other treatment.

OUTCOME AND FOLLOW-UP

Within 10 days of ingesting boxelder maple (*A negundo*) cuttings, seven fallow deer (*Dama dama*) died or had to be euthanased after showing various signs of colic, anorexia, hypothermia, shivering, increased respiratory rate and severe depression. Another fallow deer and two goats simultaneously displayed colic signs but survived.

DISCUSSION

In maple leaf intoxication, clinical signs depend on the amount of toxin ingested and include depression, polypnoea, tachycardia, pale or cyanotic mucous membranes, icterus and brown discoloration of urine.[1 2] Administration of 1.5 g red maple leaves per kg body weight proved to be toxic in ponies.[1] Postmortem lesions are related to severe hypoxia and include centrilobular hepatic degeneration, icterus, haemoglobinuric nephrosis and extensive erythrophagocytosis in the spleen and liver.[1]

Extracts from other maple species than red maple, such as silver maple (*A saccharinum)* and sugar maple (*A saccharum))* also induce haemolysis of equine erythrocytes.[5] Wilted or dried leaves are more toxic than freshly harvested non-dried leaves.[1 9]

In horses, maple (*Acer* species) ingestion may induce two separate intoxications. Whereas boxelder tree seed ingestion

may inflict MADD in horses characterised by severe myopathy and presence of toxic hypoglycin metabolites in urine, in these fallow deer muscles were unaffected and these metabolites were not detected. Instead, renal failure (all deer) and haemolysis (two deer), were more consistent with maple leaf ingestion than with described hypoclycin A intoxication from box elder tree seeds. Therefore, in non-equids such as these ruminants, boxelder tree intoxication may induce a syndrome equivalent to maple leaf ingestion and not hypoglycin A-associated myopathy as in the horse. As no test is available to identify the presence of toxin in suspected maple leaf intoxication, the diagnosis remains presumptive.

In the deer, renal failure indicated by renal tubular necrosis, haemorrhages and haemolysis was consistent with severe hypoxia occurring in maple leaf intoxication. Lung oedema present in all deer may be related to hypoxia, and once present, aggravated hypoxia-related events. Unfortunately, methaemoglobinuria could not be investigated in these deer.[2]

High susceptibility of horses to maple leaf-related toxins, resulting in methaemoglobinuria, may possibly be caused by their decreased capacity to reduce methaemoglobin.[5] Similarly, methaemoglobin reducing ability of non-equids may become exhausted by sufficiently high toxin levels.

The fallow deer developed clinical signs up to seven days after ingestion of the maple cuttings and these lasted up to three days before spontaneous death or euthanasia. These subacute lethal cases were consistent with renal failure likely induced by a single toxic exposure as the cuttings were removed at an early stage. Also, individual differences in toxin ingestion may result in immediate death, disease with recovery or disease with late fatal outcome due to progressive kidney failure. This highlights the importance of a comprehensive dietary history in order to discover potential maple intoxication.

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REFERENCES

1 George LW, Divers TJ, Mahaffey EA, *et al*. Heinz body anemia and methemoglobinemia in ponies given red maple (acer rubrum L.) leaves. *Vet Pathol* 1982;19:521–33.
2 Alward A, Corriher CA, Barton MH, *et al*. Red maple (Acer rubrum) leaf toxicosis in horses: a retrospective study of 32 cases. *J Vet Intern Med* 2006;20:1197–201.
3 Westermann CM, van Leeuwen R, van Raamsdonk LW, *et al*. Hypoglycin a concentrations in maple tree species in the Netherlands and the occurrence of atypical myopathy in horses. *J Vet Intern Med* 2016;30:880–4.
4 Valberg SJ, Sponseller BT, Hegeman AD, *et al*. Seasonal pasture myopathy/atypical myopathy in North America associated with ingestion of hypoglycin A within seeds of the box elder tree. *Equine Vet J* 2013;45:419–26.
5 Boyer JD, Breeden DC, Brown DL. Isolation, identification, and characterization of compounds from acer rubrum capable of oxidizing equine erythrocytes. *Am J Vet Res* 2002;63:604–10.
6 van der Kolk JH, Wijnberg ID, Westermann CM, *et al*. Equine acquired multiple acyl-CoA dehydrogenase deficiency (MADD) in 14 horses associated with ingestion of maple leaves (Acer pseudoplatanus) covered with European tar spot (Rhytisma acerinum). *Mol Genet Metab* 2010;101:289–91.
7 Dewitt SF, Bedenice D, Mazan MR. Hemolysis and Heinz body formation associated with ingestion of red maple leaves in two alpacas. *J Am Vet Med Assoc* 2004;225:578–83.
8 Weber M, Miller RE. Presumptive red maple (Acer rubrum) toxicosis in Grevy's zebra (Equus grevyi). *J Zoo Wildl Med* 1997;28:105–8.
9 Agrawal K, Ebel JG, Altier C, *et al*. Identification of protoxins and a microbial basis for red maple (Acer rubrum) toxicosis in equines. *J Vet Diagn Invest* 2013;25:112–9.

Veterinary Record casereports

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