# Atypical myopathy in a horse: first confirmed case in Slovakia

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**Abstract**

Atypical myopathy is an acute and often fatal rhabdomyolysis occurring in grazing horses, caused by ingestion of hypoglycin A, a toxin detected in the seeds and seedlings of sycamore trees. This article describes a case of atypical myopathy in a two-year-old Haflinger colt with clinical signs of weakness, muscle tremors, recumbency and esophageal obstruction. Despite intensive care, the clinical status deteriorated and given the poor prognosis, the horse was euthanized. Diagnosis of atypical myopathy was confirmed by increased concentrations of hypoglycin A and methylenecyclopropyl acetic acid (MCPA)-carnitine in the serum. Atypical myopathy has been recognized in many European countries. To the authors' knowledge, this is the first confirmed case reported in Slovakia.

*Hypoglycin A, MCPA-carnitine, sycamore, Haflinger, rhabdomyolysis, esophageal obstruction*

Atypical myopathy (AM), also known as atypical myoglobinuria, is an acute and often fatal rhabdomyolysis occurring in grazing horses, especially during autumn and spring (Votion and Serteyn 2008). The disease causes an acute degeneration of skeletal muscle and is clinically characterized by weakness, stiffness, recumbency, and a mortality rate of approximately 70% (Votion and Serteyn 2008; Verheyen et al. 2012). Affected horses are predominantly young (< 3 years of age) and in good body condition (Votion et al. 2007a). Atypical myopathy is caused by ingestion of hypoglycin A, a toxin causing mitochondrial damage and multiple acyl-CoA dehydrogenase deficiencies (MADD) (Wastermann et al. 2008; Van der Kolk at al. 2010). A recent study showed that methylenecyclopropylglycine (MCPG) and its active metabolites are also involved in the development of typical AM symptoms by inhibiting enzymes that participate in β-oxidation and energy production from fat (Bochnia et al. 2019). These substances have been detected in the seeds and seedlings of the box elder tree (*Acer negundo*), sycamore maple tree (*Acer pseudoplatanus*) and in the fruits of the ackee tree (*Blighia sapida*) (Van der Kolk at al. 2010; Sander at al. 2016; Bochnia et al. 2019). Hypoglycin A is converted *in vivo* to methylenecyclopropyl acetic acid (MCPA), which is then conjugated with carnitine and glycine. Acute AM may be diagnosed by quantifying hypoglycin A, MCPA and acyl conjugates in urine and serum (Sander at al. 2016; Bochnia et al. 2019). Treatment of acute cases is only supportive and includes fluid therapy, restoration of acid-base and/or electrolyte imbalance, analgesics, dimethylsulphoxide (DMSO), vitamins (vitamin E, selenium, vitamin C), proper bedding and a warm environment (Votion and Serteyn 2008; Van Galen and Votion 2013; Valberg 2018).

## Case report

A two-year-old Haflinger colt was found lying in a field with bilateral nasal discharge, cough and weakness. After multiple attempts, the horse managed to stand and was transported to the Clinic of Horses in Košice on the same day (10th November). At arrival,

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the horse was in lateral recumbency, apathetic, and minimally responsive. Bilateral nasal discharge with food material, tachypnea, hypothermia (36 °C), mydriasis, dark pink mucous membrane with capillary refill time of 4 s were present. At auscultation crackles in the lung area were audible, peristalsis was absent, auscultation of the heart was normal. Blood lactate was measured to be 13 mmol/l, haematology was within the normal range. Biochemistry revealed mild hyperglycaemia – glucose 12.55 mmol/l (ref. range 3.56–8.34), mild hypocalcaemia – total calcium 1.76 mmol/l (ref. range 2.60–3.22), and increased serum activity of muscle enzymes: creatine kinase (CK) 1641 μkat/l (ref. range 0.83–3.33), aspartate transaminase (AST) 120 μkat/l (ref. range 3.33–6.66), lactate dehydrogenase (LDH) 79.5 μkat/l (ref. range 0.2–6.8). Electrolytes were within normal ranges.

The horse was moved in lateral recumbency to the box and after multiple attempts, he was able to stand. While standing, the patient looked nervous, weak, trembling, with lowered head and extended neck. Respiratory distress and cough were also evident. Urination was spontaneous, with dark brown urine, compatible with myoglobinuria. At palpation muscles were neither firm nor painful. The horse had no history of recent exercise. The owner stated that no sycamore trees were on the pasture or nearby and the horse had no access to food other than hay and grass. Co-grazers (2 Haflingers and 2 warmblood horses) were clinically healthy with no noticeable clinical signs.

An intravenous catheter was placed and intravenous fluids were administered. A nasogastric tube was placed but it was advanced in the oesophagus only 10 cm before encountering a resistance. An attempt was made to gently advance the impacted material towards the stomach but was unsuccessful. The horse was then sedated with xylazine (0.5 mg/kg Rometar, Bioveta A.S., Ivanovice na Hané, Czech Republic) and butorphanol (0.02 mg/kg Butomidor, Ricketer Pharma AG, Wels, Austria) and oesophagoscopy was performed. Endoscopy of the oesophagus showed impacted food material (hay) caudal to the pharynx, which was the impaction that prevented the endoscope to be advanced further into the esophagus. Endoscopy of the respiratory tract revealed food contamination and hyperaemic tracheal mucosa.

Flunixin meglumine (1.1 mg/kg Flunixin, Norbrook Laboratories, Monaghan, Ireland) and oxytocin (0.22 IU/kg, Oxytocin, Biovet JSC, Peshtera, Bulgaria) diluted in 500 ml of saline were administered intravenously and the oesophagus was lavaged with warm water through a nasogastric tube. After several unsuccessful lavage attempts, the horse laid in lateral recumbency. N-butylscopolammonium bromide (0.3 mg/kg Buscopan, Ipsen Consumer HealthCare, Boulogne-Billancourt, France) was administered intravenously. With the patient standing, esophageal lavage was performed again under sedation without improvement. The horse started to show signs of discomfort and lay again in lateral recumbency. Catheterization of the urinary bladder was performed to facilitate urination. The horse then became normothermic but unable to stand. Mucous membranes were hyperaemic with capillary refill time (CRT) 4 s, blood lactate decreased to 2.9 mmol/l, appetite remained unaffected. Infusion therapy was continued, flunixin meglumine, 2% DMSO solution and 500 ml of a multivitamin preparation with electrolytes (Duphalyte, Zoetis s.r.o., Praha, Czech Republic) were administered. The side of recumbency was changed every 4 h. Despite intensive and aggressive treatment, the clinical status of the horse deteriorated and given the poor prognosis, the owner agreed to euthanasia.

## Laboratory results

A sample of jugular whole blood was collected immediately before euthanasia. After centrifugation, the serum was refrigerated and sent to the laboratory (Laboklin s.r.o., Karlova Ves, Slovakia) for quantification of hypoglycin A and MCPA-carnitin. An increased concentration of hypoglycin A (284.1 nmol/l) and MCPA-carnitin

(119.4 nmol/l) was found in the serum (ref. range for both < 0.5 nmol/l). These findings support the diagnosis of hypoglycin A toxicity. Although clinically healthy, increased activity of muscle enzymes was found the following day in the serum of all co-grazing horses on the pasture. Hypoglycin A and MCPA-carnitin were not quantified in co-grazers because of financial restraints.

## Discussion

At arrival, the clinical signs of the horse were consistent with primary esophageal obstruction. However, the weakness, dark urine, and major increase in muscle enzyme activity indicated that the obstruction was secondary to a more severe pathology. The differential diagnoses included the acute form of grass sickness, botulism, tetanus, equine herpesvirus, myositis as well as toxic, nutritional, ischaemic, or neurogenic myopathies (Harris 1996; Palencia and Rivero 2007; Valberg 2018). Although the owner denied the presence of sycamore trees on the pasture, the high serum levels of hypoglycin A and MCPA-carnitin are consistent with ingestion of hypoglycin A-containing plants. It is possible that some seeds and/or seedlings were carried to the pasture by the wind and went undetected. Values reported for hypoglycin A and MCPA-carnitin by previous studies varied from 87.8 to 8493.8 µg/l and from 0.60 to 1.18 µmol/l, respectively (Bochnia et al. 2015; Carlier et al. 2015; Sander et al. 2016). In our case, measured hypoglycin A was 284.1 nmol/l corresponding to 40.11 µg/l and measured MCPA-carnitin was 119.4 nmol/l (0.1194 µmol/l). The relatively low values in our patient could be related to the fact that serum was collected after intensive fluid therapy. However, as laboratory results take time to be processed, the decision for euthanasia was based on clinical signs and financial restraint.

Atypical myopathy shows a temporal occurrence with most cases observed in autumn and, more sporadically, in spring. Geographic and meteorological characteristics (high humidity, marked drop in the temperature, absence of severe frost, windy/stormy days) play an important role in the development of the disease (Moussu et al. 2003). Unfavourable weather may cause stress and induce a metabolic imbalance, predisposing animals to AM. Specific climatic conditions may be another predisposing factor for the plant to exert its toxicity as it may become more palatable or undergo metabolic changes that induce toxicity (Votion and Serteyn 2008). Affected horses are predominantly young (< 3 years of age) females, in good or poor body condition, not in training, and kept on pasture (Votion et al. 2007a). However, this prevalence may just be a reflection of the horse population on pasture rather than a real predisposition (Votion et al. 2007b). A breed predisposition has not been confirmed, but cases of AM in rustic breeds (Norvegian Fjord ponies, Haflinger) are frequently reported (Delguste et al. 2002; Votion and Serteyn 2008). A case of a new-born Haflinger foal with AM has also been described (Karlíková et al. 2018). Atypical myopathy clinically manifests as an acute rhabdomyolysis, e.g. weakness, recumbency, myoglobinuria, depression, tremors and dyspnoea. Less frequently, horses show signs of a colic, dysphagia, and cardiac arrhythmias and/or murmurs (Votion and Serteyn 2008). The oesophageal obstruction can be explained by damage to the oesophageal muscle capable of impairing oesophageal peristalsis.

Several clinical signs, biochemical indices, and acylcarnitine profiles have been identified to predict survival. Based on these results, a scoring system has been developed to help clinicians with management decisions including euthanasia (Boemer et al. 2017). Elevation of muscle enzyme activity in clinically healthy co-grazing horses is a common finding (Baise et al. 2016). The elevation is less marked than in horses with clinical signs. This finding suggests the existence of a subclinical form of AM, likely due to a dose-dependent effect of the toxin and/or individual susceptibility (Delguste

et al. 2002; Baise et al. 2016). Atypical myopathy has now been recognized in many European countries (Votion 2012). However, to the authors' knowledge, no cases have previously been reported in Slovakia. Since no specific antidote for AM currently exists, prevention is key. Communication with horse owners and highlighting the threat of presence of plants on the pasture that may be toxic for horses is of vital importance.

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