Should veterinarians consider acrylamide that potentially occurs in starch-rich foodstuffs as a neurotoxin in dogs?

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ABSTRACT

Three clinically healthy Labrador puppies developed ataxia, hypermetria and convulsions shortly after eating the burnt crust of maize porridge. Two of the puppies died. Acrylamide toxicity was considered based on the history of all 3 puppies developing nervous signs after being exposed to a starch-based foodstuff that was subjected to high temperature during preparation. Acrylamide-induced neurotoxicity is thought to partially result from a distal axonopathy.

Keywords: acrylamide, ataxia, convulsions, distal axonopathy, high temperature, hypermetria, starch.

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INTRODUCTION

The presence of acrylamide, a potentially toxic substance, was only discovered in starch-rich foodstuffs as recently as 2002. The synthesis of acrylamide in starch-containing foods such as potatoes, cereals and bread is dependent on exposure to high temperatures[10]. The risk this compound poses to the consumer at the concentrations that occur in regularly consumed foodstuffs is still being debated, but prompted the European Chemical Agency to add acrylamide to the list of substances of very high concern in 2010[4].

The acrylamide monomer is a potent neurotoxin that has been known for over 50 years. Numerous toxicity trials have been conducted in mammals, including dogs.

The acrylamide monomer is a white, odourless, crystalline solid at room temperature and is used to produce non-toxic poly-acrylamide polymers. These polymers have multiple industrial uses, among others in wastewater treatment and the textile industry[2].

The toxic effect and subsequent clinical manifestation depend on the degree of exposure to acrylamide. The clinical neurological signs are attributed to a distal axonopathy, otherwise known as a 'dying-back' neuropathy[9,11,13].

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Clinical signs reported in humans after acute acrylamide exposure include sweating, nausea, myalgia, speech disorders, numbness and weakened extremeties[2].

To the authors' knowledge there are no previous cases documented of dogs that incidentally developed acrylamide neuropathy through their daily diet, but some of the trials during which acrylamide has been intentionally administered to domestic animals are discussed. The effects of acrylamide administration in dogs were found to be similar than those observed in other species[12].

CASE HISTORY

A Labrador bitch and her 3, 2-month-old puppies, all clinically healthy and in good physical condition, were fed maize porridge that was badly burnt. A day after exposure the owner reported that 1 of the puppies suffered a seizure and died. Soon afterwards another puppy started walking in an abnormal manner, vomited and had convulsions, but 24 to 48 hours after the 1st signs were noted, the puppy recovered. When the 3rd puppy started showing similar signs, the owner consulted a private veterinary practitioner.

On clinical examination the puppy was ataxic and displayed hypermetria. No other neurological signs were seen, although a full neurological examination was not done. The puppy was in good bodily condition. The temperature, pulse, respiratory parameters and mucous membrane colour were within normal limits. There was no oculonasal discharge or diarrhoea present. A blood smear showed no abnormalities and was negative for *Babesia* spp. parasites.

The veterinarian administered water-soluble vitamins (Vitamin B Co, Oberon Pharma), dexamethasone (Dexafort, Intervet Schering-Plough Animal Health) and intravenous fluid therapy. The puppy was hospitalized for observation. Despite sustained treatment the puppy's condition deteriorated. He developed tetraparesis and died 3 days later.

On *post mortem* examination a hard, black, thin, oval object 3 cm in diameter was found in the stomach. No other macroscopic lesions were noticed. The foreign object was identified as burnt porridge, which the owner fed to the puppy a few days earlier. The dam and litter had been fed porridge before and could have been exposed to burnt remnants on previous occasions.

DISCUSSION

All the puppies in this litter exhibited similar neurological signs in a short period , and either intoxication or the involvement of an infectious agent were considered as the most likely differential diagnoses for their ailment.

There was no history of exposure to any exogenous neurotoxins. The clinical signs that typically accompany frequently seen organic and inorganic intoxications in dogs (including methaldehyde, strychnine and tremogenic mycotoxins) were absent[3]. The typical haematological pathology seen in lead poisoning was not present on the blood smear. The puppies' daily diet included a good commercial puppy feed, making a thiamine deficiency unlikely. The involvement of neurotropic infectious agents causing diffuse neurological signs were ruled out as unlikely based on history and clinical examination. The following agents were excluded:

- *Toxocara canis:* although ascarid toxaemia is a likely diagnosis in this case, none of the puppies showed any other signs of worm infestation prior to eating the burnt maize porridge, no worms were present in the puppy on which a *post mortem* was performed, and the dam was dewormed shortly before whelping.

- *Neospora caninum*: neither the dam nor the puppies had any exposure to bovine placental tissue, neosporosis has never been diagnosed in cattle of the surrounding farming community, and the dam had whelped and raised normal puppies before.
- *Toxoplasma gondii*: this parasite is more commonly seen in immunosuppressed animals and less likely in dogs, and the more commonly seen respiratory and gastrointestinal signs accompanying toxoplamosis were not observed in these puppies. The classic neurological sign of hyperextended pelvic limbs seen in young animals suffering from toxoplamosis or neosporosis were absent in all 3 puppies[3].
- Distemper virus: although the puppies had not yet received their 1st inoculation prior to the development of clinical signs, the dam was fully vaccinated, and the clinical signs that typically precede neurological signs in puppies infected with distemper virus after birth were not present[3].

It is nevertheless a limitation of this report that no tests were done to confirm the absence of the abovementioned differential diagnoses.

Acrylamide toxicity

Acrylamide is well absorbed by most routes, but exposure usually occurs through oral intake or contact with the skin. The monomer is distributed widely throughout the body and metabolized by the liver to non-toxic metabolites, which are mainly excreted in the urine[9]. Studies have demonstrated rapid and large-scale absorption in dogs after oral intake of acrylamide[6]. The resulting neuropathy and the severity of the syndrome that follows intoxication are dependent on the magnitude of the dose, the rate of administration and the period of exposure to the toxin[11]. The peripheral (motor and sensory) and central nervous systems are affected, but the latter seems to require higher doses of toxin. The neuropathy is widely accepted to be an example of a central–peripheral distal axonopathy[13]. This is defined as a process whereby the distal portion of the longest peripheral axons is affected 1st, but after continuous exposure the distal segments of corticospinal, spinocerebellar and dorsal column axons also become involved. Ataxia resulting from cerebellar dysfunction follows owing to afferent and efferent cerebellar- and Purkinje fibre degeneration[1,11]. More recent studies suggest that terminal degeneration might be the primary site of pathology and precedes axonopathy[8]. With high-level acute acrylamide exposure, however, the clinical picture is typically an encephalopathy with accompanying ataxia and seizures, followed by a peripheral neuropathy. Widespread autonomic dysfunction can occur[11]. Acrylamide also has an effect on calmodulin (CaM) concentration and protein kinase C (PKC) activity, offering a hypothesis that this may be another mechanism whereby acrylamide induces neuropathy[14].

Earlier studies in cats revealed severe tonic-clonic convulsions and other signs of a diffuse central nervous excitation when lethal doses (100 mg/kg adult feline) of acrylamide monomer were administered intravenously. Administration of sublethal doses induced ataxia and tremors[7]. When adult male Beagle dogs and miniature pigs were fed 1 mg acrylamide/kg/day in the diet for 3–4 weeks no neurotoxic signs were elicited, but acrylamide was present in muscle tissue collected at *post mortem* examination. Although the nervous system is the primary target for the acrylamide monomer, less than 1 % of the substance was detected in the brain. Neuropathy was observed in the dogs and pigs when the acrylamide was administered at 5 mg/kg/day for an extended period of 30 to 60 days[6]. Chronic exposure in dogs leads to the typical progressive sensorimotor peripheral neuropathy, including toe cuffing and ataxia and weakness, with a unique association to megaoesophagus due to vagal nerve axonopathy[12]. When sublethal doses of acrylamide are discontinued, the neuropathy that developed may resolve slowly. More severe deficits like spasticity and cerebellar ataxia are likely to remain[1,9].

The most prominent histological finding in acrylamide neuropathy is degeneration of peripheral nerves[2]. Chemical analysis of tissue samples, for example muscle, could aid in the diagnosis of acrylamide poisoning. In addition to neuropathy, carcinogenicity, mutagenicity and reproductive toxicity have also been demonstrated in rats[2, 13].

The LD_{50} in rats is 100–150 mg/kg[13]. The LD_{50} in cats and monkeys was determined to range between 100 and 200 mg/kg after a single dose[2].

Quantitative food surveys done in the UK in recent years revealed that cereal can contain up to 57 mg/kg acrylamide and a kilogram of potatoes up to 112 mg[5]. Levels appear to rise as food is heated for longer periods of time. To the authors' knowledge there are no figures available for the levels of acrylamide that can be present in maize porridge exposed to high temperatures for a prolonged period.

Despite strong circumstantial evidence, it is a limitation of this report that tissue sampling for histopathology or determining tissue levels of acrylamide were not done in order to confirm the suspected acrylamide toxicity.

CONCLUSION

Porridge prepared from maize meal is a staple diet for people in South Africa and the burnt remnants are often fed to household pets. The possibility of acrylamide toxicity occurring in these animals, in particular immature animals, deserves consideration and should not be ignored when neurological cases are seen. Further studies are needed to quantify the risk acrylamide in foodstuffs poses to dogs.

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