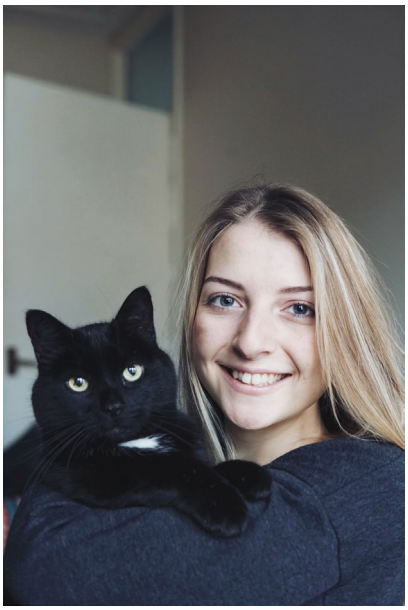

Nursing a canine with presumptive tremorgenic mycotoxicosis following ingestion of mouldy dog food – a case report

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ABSTRACT: A one-year-old neutered female Labrador Retriever presented with twitches and subsequent generalised tonic–clonic seizure activity following ingestion of mouldy dog food. Further complicating factors were hyperthermia and metabolic acidosis. Initial emergency treatment involved seizure management, blood analysis, intravenous fluid therapy, active cooling and decontamination via gastric lavage, administration of activated charcoal and an intralipid infusion. The patient was maintained under general anaesthesia to manage the seizure activity. Post-anaesthetic management included treatment of aspiration pneumonia, physiotherapy, intravenous fluid therapy and management of an indwelling urinary catheter. The patient was discharged 48 h post-admission without further complication.

Keywords: Mycotoxins; seizures; hyperthermia; aspiration pneumonia; emergency; critical care

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Introduction

Mouldy food and decomposing food waste is commonly contaminated with fungi from the fungal genus *Penicillium* spp. Such fungi are known to produce a range of mycotoxins, with two major tremorgenic mycotoxins being penitrem A and roquefortine. The lipophilic nature of these substances allows them to cross the blood–brain barrier and alter the release of the excitatory neurotransmitters glutamate and aspartate and the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) (Bradford, Norris, & Smith, 1990). Clinical signs may manifest in less than 30 min or be delayed for several hours. Presentation includes weakness, emesis, increased irritability, muscle tremors, rigidity, noise sensitivity, panting and hyperthermia (Puschner, 2002). Severity can vary, but may present with opisthotonos, paddling, seizures and recumbency, and further complicating factors may be dehydration, rhabdomyolysis and metabolic acidosis (Poppenga, 2007). A history of ingestion of mouldy food, indicative clinical signs and identification of mycotoxins in samples of the food, gastrointestinal contents, urine or serum can lead to diagnosis. It is common that more than one mycotoxin will have been ingested as *Penicillium* species often coexist (Eriksen et al., 010).

Initial presentation and emergency treatment

A one-year-old neutered female Labrador Retriever presented to the hospital with twitches after eating mouldy dog food. The patient had a generalised tonic–clonic seizure in the consulting room and further presented with nystagmus,

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tachycardia (152 beats per minute), panting and a temperature above 42°C (**Table 1**). Stomach contents had also been regurgitated.

An intravenous (IV) catheter was immediately placed in the right cephalic vein and 1 mg/kg diazepam (diazepam, hameln) was given IV to control the seizure. Intravenous fluid therapy (IVFT) with isotonic crystalloids (Hartmann's, Aqupharm) was started at 4 ml/kg/h. A mask was used to deliver 100% oxygen and oxygenation status was monitored via blood gas analysis – as recommended for best accuracy (Bloor, 2013) – and a pulse oximeter. In seizuring patients, IV access should be promptly established for the administration of anti-epileptic drugs and IVFT (Lowrie, 2013) and should receive oxygen therapy via an appropriate method depending on the patient's status.

A venous blood sample was taken for gas analysis, electrolytes, biochemistry and haematology. A multiparameter monitor was attached for an electrocardiogram (ECG) and to monitor oxygen saturation (SpO_2) and non-invasive blood pressure. The ECG displayed sinus tachycardia, the patient had bounding pulses and an SpO_2 of 97%. A blood pressure reading was unobtainable with either a doppler or oscillometric monitor while seizure activity was occurring.

The patient was actively cooled by laying on a wet towel by a fan and laying cold packs in the groin area and over the neck and abdomen. The patient's temperature was taken every 15 min initially. A drop of approximately 1°C every 15 min was achieved. After 1 h the patient's temperature had reduced to 38.8°C so active cooling was stopped. Active cooling methods should be employed once a patient's core temperature reaches 40–41°C. Patients may respond very quickly and may present with a rebound hypothermia; therefore, active cooling should cease when the temperature reaches 39–39.5°C (Polton & Branscombe, 2008). Cooling, along with IVFT, is also important to minimise the risk of renal damage secondary to rhabdomyolysis induced by seizure activity or tremors (Barker, Stahl, Ensley, & Jeffery, 2013). Despite the active cooling being stopped, the patient's core temperature continued to drop to 37°C; therefore, a heat mat was used to aid thermoregulation and temperature was monitored continually.

The seizure activity resumed after 10 min following the initial diazepam dose so a further 1 mg/kg was administered IV. The patient responded poorly so consent was obtained for general anaesthesia. A propofol (Fresenius Propoven 1%, Fresenius Kabi) continuous rate infusion (CRI) was initiated at 0.4 mg/kg/min to control the seizure activity. An endotracheal tube was placed and cuffed to protect from aspiration, and to secure a patent airway for delivery of oxygen and intermittent positive-pressure ventilation (IPPV), initially at 12 breaths per minute. Apnoea persisted after starting the propofol CRI and end tidal CO_2 ($ETCO_2$) climbed to a range of 60–80 mmHg, so the patient was artificially ventilated at 19 breaths per minute on 100% oxygen. A second IV catheter was placed in the right medial saphenous vein to continue IVFT. Systolic blood pressure was 90 mmHg initially.

Co-amoxycillin clavulanic acid (Augmentin®, GlaxoSmithKline) was given at 20 mg/kg IV due to the patient regurgitating and the common complication of aspiration pneumonia in recumbent patients (Savino, Petrollini, & Hughes, 2007).

Diagnostic tests

Initial venous blood analysis revealed a slight metabolic acidosis, hyperglycaemia and elevated creatinine. Arterial blood analysis 20 min later demonstrated a worsened metabolic acidosis and reduced hyperglycaemia. Two hours later the metabolic acidosis and hyperglycaemia had improved and creatinine had normalised. The PaO_2 indicated that oxygen supplementation was adequate throughout monitoring (**Table 2**).

Seizure activity may result in hypoxia, acidosis and hyperglycaemia; however, prolonged status epilepticus may eventually result in hypoglycaemia (Vite & Long, 2007). Renal values were monitored as damage may occur from nephrotoxic mycotoxins or secondary to seizure activity (Eriksen et al., 2010). Acidaemia should be treated with IV sodium bicarbonate only if the pH is below 7.05, as adverse effects such as rebound alkalaemia, hypernatraemia and hypokalaemia may occur (Aldridge & O'Dwyer, 2013a); therefore, sodium bicarbonate was not administered in this case.

Laboratory analysis of the food eaten was declined by the owner.

Decontamination

Gastric lavage to decontaminate the stomach was performed under anaesthesia with a cuffed endotracheal tube in place, as recommended by Poppenga (2007). Activated charcoal (medicinal charcoal, J. L. Bragg's) was administered at 3 g/kg via the stomach tube to minimise absorption of the toxins. This was repeated every 4 h due to potential enterohepatic recirculation of the mycotoxins. It has been recommended to continue this for 2–3 days; however, patients rarely show clinical signs for this long (Barker et al., 2013). Therefore, the charcoal was to be continued until the patient was passing black faeces. The poor mentation and seizure activity of the patient upon initial presentation meant inducing emesis was not appropriate due to the risk of regurgitation and aspiration.

An intralipid (Intralipid® 20%, Fresenius Kabi) infusion was administered with an initial bolus of 1.5 ml/kg over 15 min then 0.25 ml/kg/min for 60 min. The use of IV intralipid infusions have proven useful in reversing the effects of fat-soluble toxins in both human medicine (Patil, 2011) and veterinary medicine (Epstein & Hollingsworth, 2013; Sines, 2016). Fat droplets present in the plasma form a separate lipid compartment in which lipophilic toxins may dissolve, known as the lipid sink theory (Robben & Dijkman, 2017).

Table 1. Normal canine physiological reference intervals (Dallas & Ackerman, 2016; McMillan, 2016).

Parameter	Reference interval
Temperaure (°C)	38.3–38.7
Heart rate (beats/min)	60–180
Respiration (breaths/min)	10–30
Capillary refill time (s)	< 2.5
SpO_2 (%)	95–100
$ETCO_2$ (mmHg)	35–45
Systolic blood pressure (mmHg)	90–120
Mean arterial blood pressure (mmHg)	60–90
Diastolic blood pressure (mmHg)	55–75

Table 2. Blood analysis results and normal canine blood parameters. Reference intervals quoted from the epoc Veterinary Blood Gas, Electrolyte and Critical Care Analyser used in-house.

Value	Initial venous sample upon admission	Arterial sample 20 min later	Arterial sample 2 h later	Reference interval
pH	7.34	7.18	7.3	7.35–7.45
$PaCO_2$ (mmHg)	x	69	46.8	34–40
PaO_2 (mmHg)	x	249.3	335.1	85–100
HCO_3^- (mmol/l)	21.4	26	25.2	18–24
Lactate (mmol/l)	9.78	6.03	0.99	0.6–2.9
Haematocrit (%)	57	49	43	35–50
Blood glucose (mmol/l)	8.8	6.4	5.7	3.3–6.4
Creatinine (µmol/l)	139	101	92	44–115

Management under anaesthesia

Seizure activity fully subsided after beginning the propofol CRI. The patient was put on a padded bed in sternal recumbency to minimise atelectasis and aid ventilation and perfusion (Savino et al., 2007) (**Figure 1**). The patient's heart rate and rhythm, pulse quality, blood pressure, $ETCO_2$, SpO_2, temperature, mucous membrane colour, capillary refill time and eye position were continuously monitored and recorded every 5 min. Blood glucose was checked, the patient's eyes were lubricated with a carbomer lubricant (Lubrithal™, Dechra) and the oral mucosa moistened with water every hour.

$ETCO_2$ reduced to 45–50 mmHg with ventilation and the pulse rate reduced, eventually to 110–130 beats per minute. Systolic blood pressure improved with IVFT, which was reduced to 2 ml/kg/h when the systolic pressure reached 140 mmHg. SpO_2 remained over 95% throughout.

An indwelling Foley urinary catheter was placed and assessed every 4 h. Urine output (UOP) remained normal at 1–2 ml/kg/h (Aldridge & O'Dwyer, 2013b). Monitoring and maintaining hydration and UOP is key in intoxicated patients (Poppenga, 2007).

Two doses of methocarbamol (methocarbamol, Recordati) were administered via a stomach tube at 82 mg/kg to aid muscle relaxation. The patient was also put on a midazolam (Hypnovel®, Roche) CRI at 0.3 mg/kg/h, allowing the propofol CRI to be reduced to 0.2 mg/kg/h without the return of muscle tremors. The patient's blood glucose dropped to 2.7 mmol/l so 5 ml glucose (glucose intravenous infusion 50%, hameln) was administered intravenously over 10 min. This increased the blood glucose to 6.1 mmol/l, which then remained stable between 5 and 6 mmol/l.

Figure 1. The patient was maintained in sternal recumbency to aid respiratory function.

The patient was gradually weaned off artificial ventilation and the propofol CRI while observing for the return of muscle tremors. Use of the ventilator was resumed if the patient was unable to maintain adequate ventilation; however, a respiratory rate of 20–35 breaths per minute was eventually maintained unaided, $ETCO_2$ maintained at 35–45 mmHg and SpO_2 over 95%. Mild tremors returned when the propofol CRI was stopped; however, this gradually subsided. The endotracheal tube was left in place until the patient was of adequate mentation. The patient remained on an ECG and pulse oximeter. All vitals were monitored and lung fields auscultated to assess for changes in lung sounds that may indicate aspiration pneumonia. The total duration of general anaesthesia was approximately 10 h.

Recovery following anaesthesia

When the patient's temperature reached 38.5°C the heat mat was turned off. Over the next 12 h the temperature climbed to 39.4°C, indicating possible pyrexia secondary to aspiration pneumonia. The patient had nasal discharge and developed a productive cough that induced several episodes of vomiting. Light crackles were heard on lung auscultation. Thoracic coupage and nebulisation with sterile saline were performed every 4 h and antibiotic therapy continued as per the recommended treatment for aspiration pneumonia (Waddell & King, 2007). Oxygen supplementation is also recommended if required (Waddell & King, 2007); however, the SpO_2 remained over 95% without supplementation. The clinical signs subsided 36 h post-recovery, but as the patient improved, she became less tolerant of nebulisation and coupage; 1 mg/kg maropitant (Cerenia®, Pfizer) was administered IV to reduce nausea.

When the muscle tremors had fully subsided, the midazolam CRI was stopped.

The patient was non-ambulatory with hypertonia of the limbs. Massage was performed on each limb every 4 h to alleviate pain and rigidity and improve circulation and lymphatic drainage. Passive range of motion was then performed to protect against stiffening and also improve local circulation (Sims, Waldron, & Marcellin-Little, 2015). The patient was turned to the alternate lateral recumbency every 4 h. This was well tolerated and the patient was able to support herself in sternal recumbency and ambulate with sling support 12 h later (**Figure 2**).

The patient was maintained on 4 ml/kg/h isotonic crystalloid IVFT throughout recovery to replace losses from vomiting. IV catheter patency and the surrounding site were checked several times a day for complications such as infection, thrombophlebitis or extravasation of fluid (Aldridge & O'Dwyer, 2013c). During recovery, oedema formed proximal to the IV catheter site of the right hind limb. Assessment of the IV catheter showed it had become displaced and fluid was being delivered subcutaneously. The catheter was removed and massage and cold compress of the area was performed every 4 h until the swelling had reduced.

UOP remained within normal limits and the urinary catheter was removed when the patient was able to ambulate outside.

Figure 2. The patient was bright and alert and could support herself in sternal recumbency 12 h post-anaesthetic.

As the patient had been vomiting, a bland wet diet was fed in small meals when the patient was of adequate mentation and the risk of further seizures low. Nutritional support is crucial in critically ill patients; however, it is important to address other factors such as dehydration, electrolyte and acid–base disturbances before devising a nutritional plan (Chan, 2006).

Blood biochemistry results were all within normal limits following recovery, including urea and creatinine. Meloxicam 0.2 mg/kg (Metacam®, Boehringer Ingelheim) was administered subcutaneously then continued orally at 0.1 mg/kg every 24 h. Ten-day courses of 17.48 mg/kg oral metronidazole (Metrobactin®, Dechra) and 17.48 mg/kg amoxycillin and clavulanic acid (Clavaseptin®, Vétoquinol) were also started.

Discharge

The patient was discharged 48 h post-admission. She was bright and bouncy, clinical signs of aspiration pneumonia had subsided and she was ambulatory without support. Slight oedema and bruising of the medial right hind limb was still present so the owner was advised to apply a cold compress for 10 min twice daily. The owners were shown how to deliver thoracic coupage several times a day.

The patient was seen 5 days later for a check-up. Besides being quieter at home for the first 24–36 h, she was back to her normal self with no neurological signs or respiratory signs associated with aspiration pneumonia. Oedema of the leg had reduced and oral medication was being taken well. After completing all courses of medication, the patient continued to be clinically well at home with no complications noted.

Most patients have a good prognosis and recover from mycotoxin ingestion within 24–48 h without sequelae if decontamination is commenced soon after exposure (Puschner, 2002). Rapid decontamination, treatment of complicating factors and meticulous monitoring in this particular case meant for a successful outcome and very happy owners.

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