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Short Communication

Metabolic and toxic causes of canine seizure disorders: A retrospective study of 96 cases

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ABSTRACT

A wide variety of intoxications and abnormal metabolic conditions can lead to reactive seizures in dogs. Patient records of dogs suffering from seizure disorders ($n = 877$) were reviewed, and 96 cases were associated with an underlying metabolic or toxic aetiology. These included intoxications by various agents, hypoglycaemia, electrolyte disorders, hepatic encephalopathy, hypothyroidism, uraemic encephalopathy, hypoxia and hyperglycaemia. The incidence of the underlying diseases was determined.

The most common causes of reactive seizures were intoxications (39%, 37 dogs) and hypoglycaemia (32%, 31 dogs). Hypocalcaemia was the most frequent electrolyte disorder causing reactive seizures (5%) and all five of these dogs had ionised calcium concentrations ⩽0.69 mmol/L. Eleven per cent of dogs with seizures had metabolic or toxic disorders and this relatively high frequency emphasises the importance of a careful clinical work-up of cases presented with seizures in order to reach a correct diagnosis and select appropriate treatment options.

Introduction

Seizures are one of the most common neurological disorders in dogs (Podell et al., 1995; Berendt, 2004). Based on aetiology, seizures have been grouped into three different categories, namely, (1) idiopathic, (2) symptomatic and (3) reactive (Podell, 1996). A status of recurrent seizures is defined as epilepsy (Berendt, 2004). Reactive seizures have an extracranial origin, can be caused by a variety of metabolic disturbances and intoxications (O'Brien, 1998), and can be elicited by dysfunction of virtually any organ system (Boggs, 1997). Possible differential diagnoses are summarised in Table 1 (Cunningham, 1971; Fuhrer, 1990; Steffen and Jaggy, 1995; O'Brien, 1998). Most of these conditions are reversible depending on the underlying disease so permanent antiepileptic drug therapy should only be initiated when the seizures are uncontrolled despite therapy or when an emergency situation such as status epilepticus occurs (Boggs, 1997). In the current study, the frequency of various aetiologies of reactive seizures in dogs was evaluated.

A total of 877 patient records of dogs were reviewed for underlying metabolic or toxic disturbances. The dogs had seizure disorders and were presented to the Department of Small Animal Medicine and Surgery of the University of Veterinary Medicine, Hannover, between 2004 and 2008. Hypoglycaemia was considered to be the cause of the seizure when dogs showed repeated low blood glucose levels and an underlying disease (such as neoplasia) could be identified, or the when the animals presented had low blood glucose levels during a seizure and immediately responded to IV glucose administration (Podell, 2004).

Hepatic encephalopathy was diagnosed mainly through marked hyperammonaemia; diagnostic imaging of the liver and abdominal blood vessels was performed with ultrasound and/or computed tomography (Hardy, 1992). Uraemic encephalopathy was diagnosed by measuring plasma creatinine and urea concentrations and detecting an acute or chronic renal disease (Fenner, 1995). Electrolyte disorders were considered the cause of the seizure when at least one of the concentrations of calcium, sodium or potassium was markedly decreased or increased due to an underlying disease (Podell, 2004). Hypothyroidism was presumed to be responsible for the seizure disorder after evaluation with a thyro tropin-releasing-hormone stimulation test or by demonstrating elevated thyroid-stimulating hormone levels with concurrent low thyroxin levels (Jaggy, 1990; Scott-Moncrieff, 2009). In cases of presumed hypoxia, the owners reported that anaesthesia had been performed prior to presentation.

Hyperglycaemia was diagnosed when markedly elevated blood glucose levels (e.g. due to concurrent diabetes mellitus) and hyperosmolality were observed concurrently with the seizures (O'Brien, 1998). A diagnosis of intoxication was made by toxicological analysis of urine (Maurer, 2004) when a toxic material could be identified in stomach contents or faeces, when multiples cases occurred

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Table 1
Extracranial causes of seizures in dogs (adapted and modified from Cunningham (1971), Fuhrer (1990), Steffen and Jaggy (1995), and O'Brien (1998)).

Metabolic causes of seizures	Selection of toxic causes of seizures
• Hypoglycaemia	• Animal toxins
• Hypoxia	• Caffeine and other methylxanthines
• Hyperthermia	• Hydrocarbons and petroleum distillates (e.g. ethylene glycol, methanol)
• Hyperosmolality	• Lead and other heavy metals
• Hyponatraemia and hypernatraemia	• Mycotoxins
• Hypocalcaemia and hypercalcaemia	• Pesticides (e.g. bromethalin, metaldehyde, organophosphates and carbamates, pyrethrins and pyrethroids, strychnine)
• Hepatic encephalopathy	• Plant toxins
• Uraemic encephalopathy	• Drugs
• Hyperlipoproteinaemia	
• Hypothyroidism	

in the same household, or when the owners witnessed their dog ingesting possible toxic substances. Low activities of cholinesterase were used as a diagnostic measure for presumptive organophosphate or carbamate intoxication (Fikes, 1990).

A metabolic or toxic disorder (Fig. 1) was found in 96/877 (11%) of dogs with seizures. These animals were included in the study and their records were reviewed. The majority of the 96 dogs had generalised seizures with loss of consciousness (49%, 47/96). Thirty-nine dogs (41%, 39/96) were presented in status epilepticus. Thirty-one dogs (32%, 31/96) were found to be hypoglycaemic. Electrolyte disorders were responsible for seizures in 10 dogs (10%, 10/96). Hepatic encephalopathy with concurrent seizures occurred in nine dogs (9%, 9/96). Hypothyroidism was the suspected cause in three dogs (3%, 3/96). Uraemic encephalopathy (2%, 2/96), presumptive hypoxia (2%, 2/96) and hyperglycaemia (2%, 2/96) were less frequent causes of seizures. Intoxication was the most frequent diagnosis (39%, 37/96).

Different diseases were found to be the underlying cause of the hypoglycaemia (Fig. 2). Neoplasia (e.g., insulinoma, suspected insulinoma or other tumours) led to seizures in 68% (21/31) of all dogs in this group. The mean age of patients with tumours was 10 years (range 7–16 years). Five dogs (16%, 5/31) with a mean age of 3.4 months had juvenile hypoglycaemia due to various underlying causes such as starvation, gastrointestinal (GI) parasites and other GI disturbances. The mean blood glucose concentration of all dogs with hypoglycaemia at the time of presentation was 2.19 mmol/L (range 0.55–3.5 mmol/L; reference range 3.9–6.1 mmol/L).

Electrolyte disorders were responsible for seizures in 10 dogs. Of these, five showed marked hypocalcaemia with a mean ionised calcium concentration of 0.61 mmol/L (range 0.5–0.69 mmol/L; reference range 1.25–1.47 mmol/L). Hypoparathyroidism, suspected hypoparathyroidism, lactation, protein losing enteropathy

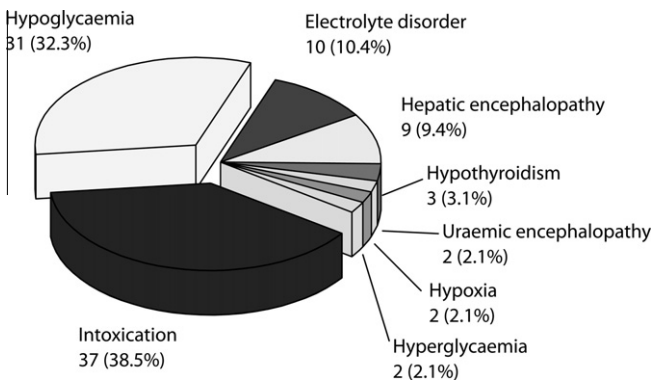

Fig. 1. Occurrence of seizures due to metabolic and toxic disturbances (n = 96). Proven and presumptive intoxications (37 dogs) and hypoglycaemia (31 dogs) were the most frequent extracranial causes for seizures.

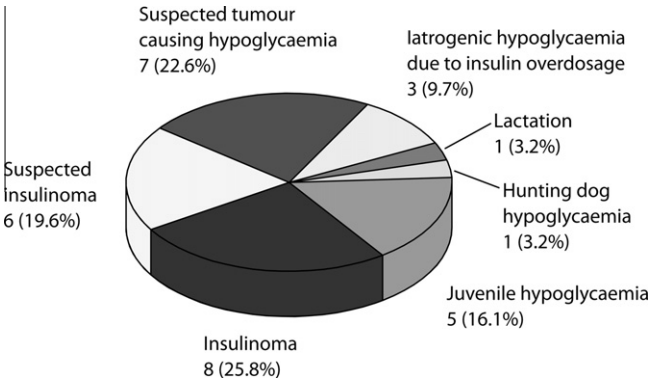

Fig. 2. Differential diagnoses for hypoglycaemia in dogs with seizures (n = 31). The most common differential diagnosis for hypoglycaemia and concurrent seizure disorders was neoplasia (21 dogs). Insulinoma was only suspected but not proven when hyperinsulinaemia and repeated low blood glucose concentrations were measured and no further diagnostic imaging procedures were performed due to owner restriction. Other tumours were suspected to induce hypoglycaemia when repeated low blood glucose concentrations were measured without concurrent hyperinsulinaemia, when neoplasms were found and, in the case of surgical removal of the tumour, when hypoglycaemia resolved after surgery.

and iatrogenic hypocalcaemia after resection of a parathyroid carcinoma were the underlying diseases. The other five dogs had Addison's disease (two dogs), overdosing of metildigoxin, excessive vomiting and severe systemic illness with marked elevation of serum potassium ion concentrations (6.46 mmol/L; reference range 3.5–5.1 mmol/L).

Hepatic encephalopathy due to portosystemic shunting occurred in nine dogs. Seven of these had seizures before surgical intervention, and two developed seizures after incomplete ligature of the shunt vessels. The mean serum ammonia concentration at presentation was 221.48 μmol/L (range 147.00–265.78 μmol/L). Two dogs were presented after general anaesthesia for routine operations performed by referring veterinarians but neither of the dogs had previously had seizures. Seizures developed in one dog subsequent to the anaesthesia, while the other developed seizures about 8 h later. Both dogs displayed partial seizures during clinical examination in our clinic. Partial oxygen pressure was normal in both dogs at the time of presentation and seizures resolved in both animals 24 h after admission. Hyperglycaemia was found in two dogs with diabetes mellitus and concurrent seizures. Blood glucose concentrations at presentation were 102.12 mmol/L and 32.19 mmol/L, respectively.

The most common diagnosis for dogs with reactive seizures was proven or presumptive intoxication. Metaldehyde (19%, 7/37) and organophosphate or carbamate poisoning (16%, 6/37) were the most frequent intoxications. The mean cholinesterase level in organophosphate or carbamate poisoning was 354 U/L (range