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Status epilepticus in dogs and cats, part 1: etiopathogenesis, epidemiology, and diagnosis

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Abstract

Objective – To review current knowledge of the etiopathogenesis, diagnosis, and consequences of status epilepticus (SE) in veterinary patients.
Data Sources – Human and veterinary literature, including clinical and laboratory research and reviews.
Etiopathogenesis – Status epilepticus is a common emergency in dogs and cats, and may be the first manifestation of a seizure disorder. It results from the failure of termination of an isolated seizure. Multiple factors are involved in SE, including initiation and maintenance of neuronal excitability, neuronal network synchronization, and brain microenvironmental contributions to ictogenesis. Underlying etiologies of epilepsy and SE in dogs and cats are generally classified as genetic (idiopathic), structural-metabolic, or unknown.
Diagnosis – Diagnosis of convulsive SE is usually made based on historical information and the nature of the seizures. Patient specific variables, such as the history, age of seizure onset, and physical and interictal neurological examination findings can help hone the rule out list, and are used to guide selection and prioritization of diagnostic tests. Electroencephalographic monitoring is routinely used in people to diagnose SE and guide patient care decisions, but is infrequently performed in veterinary medicine. Nonconvulsive status epilepticus has been recognized in veterinary patients; routine electroencephalography would aid in the diagnosis of this phenomenon in dogs and cats.
Clinical Sequelae – Status epilepticus is a medical emergency that can result in life-threatening complications involving the brain and systemic organs. Status epilepticus often requires comprehensive diagnostic testing, treatment with multiple anticonvulsant agents, and intensive supportive care.

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Keywords: canine, central nervous system, epilepsy, feline, GABA, seizure

Abbreviations

COX	cyclooxygenase
CSE	convulsive status epilepticus
EEG	electroencephalogram
GABA	γ-aminobutyric acid
HRV	heart rate variability
MRI	magnetic resonance imaging
NCSE	nonconvulsive status epilepticus
NMDA	*N*-methyl-D-aspartate
Pgp	P-glycoprotein
SE	status epilepticus
SUDEP	sudden unexpected death in epilepsy

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Introduction

An epileptic seizure is defined as hypersynchronous neuronal electrical activity in the cerebral cortex that manifests as a paroxysmal and transient abnormality of consciousness, motor activity, autonomic function, sensation, or cognition.[1] Status epilepticus (SE) is commonly defined as seizure activity that lasts for more than 5 minutes, or the occurrence of 2 or more seizures without recovery of consciousness.[1,2] Status epilepticus was initially defined as seizure activity that persisted for 20–30 minutes, or the amount of time needed to cause irreversible neuronal damage or death. However, the definition has been refined as clinicians recognized that emergency treatment was necessary before 20 minutes

has passed.[3] Status epilepticus is a life-threatening emergency that requires immediate intervention. Refractory status epilepticus is defined as SE that does not respond to first-line anticonvulsant therapy.[1,4] Superrefractory status epilepticus is defined as SE continuing or recurring more than 24 hours after initiation of treatment with anesthetic therapy.[5] Not to be confused with SE, the condition of acute repetitive seizures has been defined as the occurrence of 2 or more distinct seizures within a 24-hour period with the patient regaining consciousness between seizures. Acute repetitive seizures have also been called serial, repetitive, or crescendo seizures, and are most often called cluster seizures in veterinary medicine.[6,7]

Status epilepticus is a common neurologic emergency in people and small animals. It has been estimated that 150,000 cases of SE occur each year in people living in the United States, with 55,000 associated deaths and an estimated cost of inpatient admission of $4 billion.[4,8,9] In 1 veterinary study, the prevalence of dogs hospitalized for seizure activity and SE was 2.6% and 0.7%, respectively. Status epilepticus has been identified in 16.5% of dogs presenting to the hospital for seizure activity and was the first manifestation of a seizure disorder in 58% of dogs.[10,11]

In dogs that present in SE, prompt treatment to stop clinical and electrical seizure activity is necessary, as prolonged seizure activity has several negative systemic and neurologic consequences. Status epilepticus of longer duration is less responsive to anticonvulsant therapy compared to SE of shorter duration.[1] In addition to their potential to increase morbidity and mortality, cluster seizures and SE are disturbing for pet owners to witness.[12,13]

Pathophysiology of Status Epilepticus

Status epilepticus results from a failure to terminate seizure activity. The mechanisms that cause isolated seizure activity to progress to SE are unknown, likely multifactorial, and probably depend on the etiology of the seizure. Seizures result from spontaneous, excessive, hypersynchronous electrical discharge from a group of neurons in cortical tissue. This discharge can begin in one region of the cortex and spread to neighboring regions. Any event that disrupts the balance between neuronal excitation and inhibition can cause a seizure focus to form. In an epileptic focus, neurons undergo a sequence of events known as the paroxysmal depolarization shift. First, sustained and uninhibited neuronal depolarization may lead to the cellular influx of calcium. The calcium influx leads to opening of voltage-gated sodium channels and an influx of sodium, causing a burst of action potentials. A plateau-like depolarization occurs after the action potential burst, followed by rapid repolarization and then hyperpolarization that is mediated by γ-aminobutyric acid (GABA) receptors.[14,15] The excitability of neurons can be affected by alterations in neurotransmitter receptor function or distribution; neurotransmitter synthesis, release, or recycling; energy metabolism; or ion channel function.[16] Within minutes of initiation of seizure activity, persistent depolarization within the affected cortical region causes profound and gradual changes in local regulation. These changes are characterized by activation of second messenger systems, altered gene expression and protein production, and reorganization of synapses. The end result is irreversible cell damage and death. As the seizure continues, the epileptogenic region of the cortex can become refractory to anticonvulsant therapy.[17]

It has been proposed that SE develops due to a failure of inhibition or excessive stimulation. The major inhibitory neurotransmitter is GABA. GABA receptors are divided into 3 categories: GABA-A, GABA-B, and GABA-Aρ (formerly known as GABA-C).[18] Binding of GABA to GABA-A receptors causes chloride influx and hyperpolarization of the cell, which inhibits future action potentials. GABA-A agonists, such as benzodiazepines and barbiturates, can terminate seizure activity. It has been documented in recent years that the expression, location, and number of GABA-A receptors is dynamic and tightly regulated. The GABA-B receptor is a G-protein coupled receptor. Ligand binding to GABA-B opens potassium channels and closes calcium channels, which leads to hyperpolarization of the membrane.[4,19,20]

Studies in human and animal models have shown that the inhibitory effect of GABA is altered with time, as drugs that act at GABA receptors become less effective with prolonged seizure activity.[2,3,21–25] The diminished efficacy of GABA agonists may be related to altered receptor function or internalization of GABA receptors.[4] In epileptic rats, the expression of GABA receptor mRNA and the function of GABA receptors was found to be abnormal.[26] In mouse and rat models, SE resulted in decreased stability of GABA-A receptor subunits and reduced GABA-A receptor cell surface expression, as well as internalization and functional loss of GABA-A receptors with prolonged SE.[27,28] Further studies documented decreased surface expression of the β2/3 and γ2 GABA-A subunits.[29]

The major excitatory neurotransmitters in the central nervous system are glutamate, aspartate, and acetylcholine. The 2 main types of glutamate receptors are inotropic and metabotropic. Inotropic receptors include alpha-amino-2,3-dihydro-5-methyl-3-oxo-4-isoxazolepropanoic acid (AMPA), kainate receptors, and *N*-methyl-D-aspartate (NMDA) receptors. The influx of sodium and the efflux of potassium through inotropic

channels lead to depolarization of the membrane and action potential generation. The NMDA receptor has a calcium channel that becomes permeable to calcium during local membrane depolarization. Inward current of calcium causes further depolarization and can lead to cell death during excessive neuronal activation.[14] Metabotropic glutamate receptors use a second messenger system to increase inward currents of sodium and calcium, which leads to depolarization. Kainite, AMPA, and NMDA agonists have been shown to stimulate seizure activity.

One mechanism of drug resistance in epileptic patients is the overexpression of P-glycoprotein (Pgp). P-glycoprotein is a multidrug transport protein encoded by the gene MDR1.[30] P-glycoprotein is found in capillary endothelial cells of the blood-brain barrier.[31,32] It functions as an ATP-dependent efflux pump of several substances including antimicrobials, immunosuppressive agents, and possibly lipophilic anticonvulsant drugs.[31] It is thought that overexpression of Pgp enables resistance to anticonvulsant therapy by prohibiting uptake of these medications into the CNS at therapeutic levels.[30,32–35] Increased expression of the genes that encode for multidrug transport proteins and increased levels of Pgp have been found in drug-resistant epileptic people.[30,31,35] Additionally, it has been documented that administration of a Pgp inhibitor, tariquidar, improves the uptake of anticonvulsant drugs into the brain.[36,37] In a canine model of spontaneous SE, endothelial Pgp expression was increased by 87%–166%.[33] However, in a 2007 study in which canine osteosarcoma cells were induced to express Pgp, common anti-epileptic drugs were found to be weak substrates or not substrates for Pgp. This finding suggests that the efficacy of lipophilic anticonvulsant medications in canine epileptics may not be affected by changes in Pgp expression.[38] In 1 case of fatal SE in a person, significant upregulation of drug transporter proteins was documented in normal brain tissue and in the tissue containing the seizure focus.[39] Glutamate release during seizure activity and the signaling of glutamate at NMDA receptors and cyclooxygenase 2 (COX-2) appear to cause Pgp upregulation. Increased expression of Pgp has been documented in mouse and rat brain capillaries exposed to glutamate, and glutamate-induced upregulation of Pgp expression is blocked in the presence of a COX-2 inhibitor. Additionally, increases in Pgp during induced SE in rats were attenuated after the administration of a COX-2 inhibitor.[40]

Central nervous system damage in status epilepticus

Cerebral damage that accompanies SE is characterized by neuronal cell necrosis, gliosis, and network reorganization.[41] Prolonged seizure activity in primates has been shown to cause damage in multiple areas of the brain.[42,43] Damage to hippocampal neurons can occur even if the initiating seizure focus is not located in the hippocampus. Neuronal death is mainly mediated by excitatory neurotoxic effects. Glutaminergic receptor overstimulation leads to cellular calcium influx, which triggers a sequence of events that result in apoptosis or necrosis.[41] The events triggered by this calcium influx include immunosuppression, activation of signaling pathways that mediate apoptosis, mitochondrial dysfunction, oxidative stress, release of neurotransmitters, dendritic remodeling, and inflammatory reactions.[44] In the canine brain, it has been documented that neuronal necrosis becomes worse and more widespread the longer that SE lasts.[45,46]

Cerebral edema may also result from prolonged seizure activity. Seizure foci have high metabolic demands and increased blood flow; this hyperperfusion may disrupt the blood-brain barrier and contribute to vasogenic edema.[47–51] If the increase in blood flow does not meet metabolic demands, lactate is generated from anaerobic metabolism and may further damage the blood-brain barrier. Prolonged seizure activity in animal models led to failure of Na/K-ATPase pumps and influx of water and sodium into the cell.[52] This influx, combined with excessive glutamate release and increased membrane ion permeability, can lead to cytotoxic edema.[53,54] Cerebral edema may cause various magnetic resonance imaging (MRI) abnormalities in human epileptic patients commonly referred to as transient periictal MRI abnormalities. Transient periictal MRI abnormalities are brain MRI signal abnormalities that are attributable to seizure activity and that may be totally or partially resolved on follow-up MRI studies.[55,56] Lesions similar to transient periictal MRI abnormalities in people have also been identified in dogs with epileptic seizures.[56]

Systemic effects of status epilepticus

Status epilepticus has several systemic effects that occur in 2 phases.[57] In phase I, or compensated SE, an increase in autonomic activity occurs secondary to seizure activity. Elevated concentrations of circulating catecholamines and steroids lead to hypertension, tachycardia, hyperglycemia, hyperthermia, and ptyalism. Cerebral metabolic demand is high, and cerebral blood flow is increased to maintain oxygen delivery to the brain. Increased autonomic stimulation can cause cardiac arrhythmias, acidosis, rhabdomyolysis, hypotension, shock, noncardiogenic pulmonary edema, and acute tubular necrosis.[4]

Phase II, or uncompensated SE, begins after approximately 30 minutes of continuous seizure activity.

During this phase, cerebrovascular autoregulation fails and intracranial pressure increases.[17] Systemic hypotension and autonomic dysfunction occur, leading to decreased cerebral blood flow. The body is unable to compensate for the persistently high cerebral metabolic demand. Hypoglycemia, hyperthermia, hypoxia, respiratory failure, acidosis, hyperkalemia, hyponatremia, and uremia may occur. Hyperthermia, hypoxia, and hypotension have been shown to exacerbate the degree of neuronal injury in animal models of SE.[1,4]

Sudden unexpected death in epilepsy

Sudden unexpected death in epilepsy (SUDEP) has been defined in human epileptics as "the sudden, unexpected, witnessed or unwitnessed, nontraumatic, and nondrowning death of a patient with epilepsy with or without evidence of a seizure, excluding documented status epilepticus, and in which postmortem examination does not reveal a structural or toxicological cause of death."[58] SUDEP has been estimated to cause 2,000 human deaths in the United States annually and may be the source of 15% of all epilepsy-related deaths.[59,60] SUDEP typically occurs in patients with poorly controlled epilepsy, and current preventative measures focus on decreasing seizure frequency.

The underlying cause of SUDEP is unknown. The condition may be due to an abnormality of breathing, cardiovascular dysfunction, arousal deficits, or a combination of these.[61] Apnea and decreased oxygen saturation have been documented in patients experiencing seizure activity, and periictal hypoventilation may lead to cardiac abnormalities such as prolongation or shortening of the QT interval on the ECG.[62–64] Other cardiac dysfunction that is known to occur during seizures includes tachyarrhythmias, bradycardia, and torsades de pointes.[65,66] Heart rate variability (HRV), which results from modulation of the sinoatrial node by the autonomic nervous system, is reduced in patients with temporal lobe epilepsy compared to the general population.[67–69] Epilepsy surgery improves abnormalities in HRV and cerebrovascular autoregulation, which suggests that these may be related to seizure activity.[70] Reduced HRV has been associated with sudden cardiac death, but studies regarding its role in SUDEP have yielded conflicting results.[71–73] Several theories pose that arousal and consciousness are controlled by the ascending arousal system, a group of subcortical structures located in the upper brainstem.[74–77] The ascending arousal system is composed of discrete neurotransmitter-specific nuclei, including the raphe nuclei, the locus coeruleus, the tuberomammillary nucleus, the ventral tegmental area, the pedunculopontine and laterodorsal tegmental nuclei, and the parabrachial complex.[78–82] A seizure that propagates into the brainstem and affects these nuclei may affect the patient's level of consciousness, predisposing them to SUDEP as protective mechanisms are depressed.[61]

The MORTality in Epilepsy Monitoring Units Study (MORTEMUS) aimed to characterize events leading to SUDEP in people with epilepsy. Of 93,791 epileptic patients that were monitored, 16 cases of definite or probable SUDEP were identified along with 9 cases of "near SUDEP." All of the SUDEP and 7/9 near SUDEP events occurred after a generalized convulsive seizure. The study reported that tachypnea began after a seizure, followed by apnea, bradycardia, and postictal generalized electroencephalogram (EEG) suppression, which is profound flattening of the EEG recording that occurs after seizure activity. Apnea always occurred before terminal asystole. The majority of events (14/16) observed occurred at night, and 14 of 16 patients that died did so in a prone position. Cardiopulmonary resuscitation was successful in all cases if initiated within 3 minutes, but unsuccessful if initiated after 10 minutes. The authors of the study concluded that SUDEP was initiated by centrally mediated alteration of both respiratory and cardiac functions after generalized tonic-clonic seizures. However, the study was retrospective and no monitoring of respiratory or ventilatory function was performed.[83] SUDEP is thought to be uncommon but may be underrecognized in veterinary patients. Death during or immediately following seizure activity has been documented in epileptic dogs.[84–86] One of these patients had risk factors for SUDEP similar to those described in human epileptic patients. Considering the majority of veterinary patients in SE present with generalized tonic-clonic seizures, and the link of this seizure phenotype with SUDEP, it is plausible that mechanisms of SUDEP contribute to SE-associated mortality.[86]

Etiology and Epidemiology

The conditions that can lead to SE are the same as those underlying isolated epileptic seizures (Table 1), although the classification of epileptic seizures has been the subject of recent revision and controversy in human and veterinary medicine.[2,87,88] Genetic or idiopathic epilepsy is a well-defined entity in dogs, and a common underlying cause for SE. A hereditary basis for epilepsy has been documented in several breeds of dogs, including Labrador Retrievers, German Shepherd Dogs, Golden Retrievers, Bernese Mountain Dogs, Belgian Tervurens, Vizslas, Keeshonds, English Springer Spaniels, and Border Collies.[84–93,95] Although epileptic syndromes with a suspected genetic basis have recently been identified in cats, there is currently insufficient evidence to validate

Table 1: Suggested etiologic classification of epilepsy in veterinary patients

Past etiologic classification	Proposed ILAE etiologic classification[94,95]
Idiopathic or primary	Genetic: seizures are result of a known or presumed genetic defect.
Symptomatic or secondary	Structural-metabolic: structural or metabolic disease that is confirmed to be associated with an increased risk of developing epilepsy.
Cryptogenic	Unknown: underlying etiology unknown; could be fundamentally genetic or result from an unidentified structural or metabolic disorder.

the use of the term genetic epilepsy in that species.[88,96–98] Instead it has been suggested that the term unknown or presumptive unknown epilepsy be used in cats with epileptic seizures in which no underlying etiology can be identified.[88] Head trauma, neoplasia, meningoencephalitis, congenital malformations, intoxications, and vascular events are common etiologies of SE caused by structural-metabolic epilepsy.

Epidemiologic studies on SE in dogs are limited. A 1999 retrospective study of 156 dogs found a 0.44% prevalence of SE as a proportion of hospital admissions at a referral facility. The cause of seizures was found to be primary or genetic epilepsy in 26.8% of cases, secondary epilepsy in 35.1% of cases, reactive in 6.7%, undetermined in 25.8%, and related to low concentrations of antiepileptic drugs in 5.7%.[11] In a 2001 retrospective study of 32 dogs with presumed genetic or unknown epilepsy, 19/32 (59%) of dogs had 1 or more episodes of SE. Not all dogs in the study had advanced imaging or analysis of CSF to confirm their diagnosis of epilepsy.[98] A 2002 study of SE in dogs found that SE was more frequently associated with structural-metabolic epilepsy than with genetic/unknown epilepsy. Non-SE seizures were at least twice as likely to be due to genetic/unknown than other causes, and 44% of dogs that presented in SE had no prior documented seizure activity.[99] In a 2009 retrospective study, a higher risk for SE was found in dogs that experienced seizures secondary to toxin exposure, and these dogs did not experience seizures after discharge. In that study, 58% of dogs presented with SE as the first documented manifestation of a seizure disorder. Structural brain disease was a common cause of seizures in dogs older than 5 years, and these dogs had a lower probability of survival compared to dogs with genetic epilepsy and metabolic epileptic seizures.[10] A higher risk for development of epileptic seizures and SE has been found in spayed females compared to intact females, and no predilection for metabolic epileptic seizures was found in males, even though this has been documented previously.[2,100] A 2012 retrospective study of dogs with genetic or unknown epilepsy showed a high prevalence of cluster seizures, but a low prevalence of SE.[101] However, other studies have shown a high occurrence of SE in dogs with genetic or unknown epilepsy.[98,102]

Diagnosis of Status Epilepticus

Classification of status epilepticus by clinical appearance

In veterinary medicine, SE is typically classified based on the clinical appearance of the seizures into convulsive SE (CSE) or nonconvulsive SE (NCSE). The majority of small animals that develop SE will present with an ictal phenotype consistent with CSE, manifesting with generalized tonic-clonic movements and an impaired level of consciousness with or without autonomic manifestations.[10,11] Nonconvulsive SE is defined as EEG evidence of seizure activity without the clinical appearance associated with CSE. In people, there is a wide spectrum in the possible clinical appearances of nonconvulsive seizures that can include both positive (aggression, delusions, automatisms) and negative (aphasia, anorexia, catatonia) symptoms.[103] However, 2 primary phenotypes of NCSE have been observed in people. The first occurs in ambulatory patients who present in states of confusion with or without subtle twitches or other cognitive changes. These patients have been termed to be in "walking status" by some authors. The other manifestation occurs in patients with severely impaired level of consciousness that display very subtle, if any, overt motor manifestations of seizure activity. These patients have been referred to as the ictally comatose, and this variant of NCSE is typically called "subtle status."[104] Though NCSE is common in critically ill people, it has not been frequently documented in veterinary medicine; this discordance may reflect the underutilization of EEG in the diagnosis of epileptic seizures in dogs and cats. In a prospective study of people with altered mental status, NCSE or nonconvulsive seizures were documented in 21% of patients; 25% of these patients had prior seizures that were clinically apparent. One-half of these patients had subtle findings such as muscle twitching or eye deviation.[105] NCSE may occur before or after convulsive seizures are apparent; therefore, NCSE should be considered in any patient with a prolonged postictal state, or in an immobile patient experiencing a prolonged period of impaired consciousness following the treatment of CSE, especially after the withdrawal of anesthetics and sedatives used to control SE.[106] A high index of suspicion is especially pertinent in veterinary medicine, given that the expertise and equipment

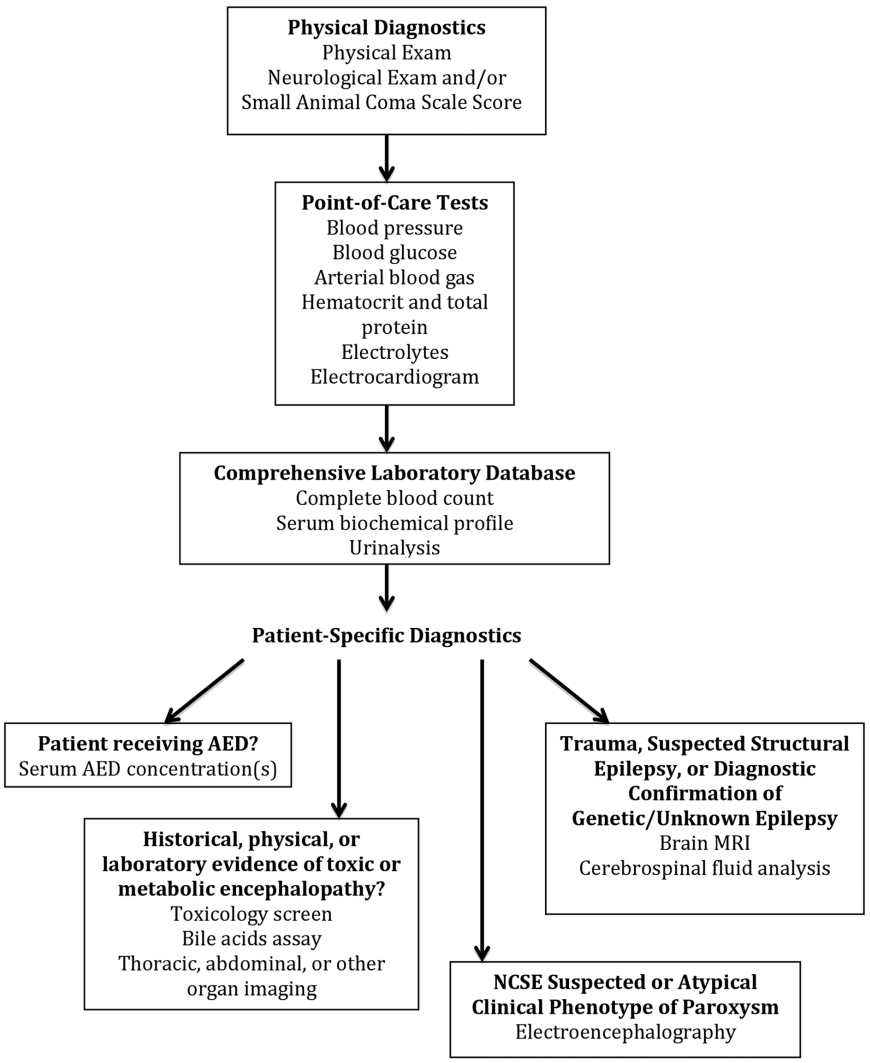

Figure 1: Diagnostic algorithm for patients with status epilepticus.

necessary for electroclinical corroboration of NCSE is often lacking.

History and signalment

The owners of dogs that present in SE should be questioned thoroughly about the patient's previous history of seizures or diagnosed neurologic disease, and whether any anticonvulsants are currently used. It is beneficial to ask about changes in behavior or abnormal clinical signs noted at home before the seizure activity began. Any other metabolic diseases that the patient has and current medications that they receive (for example, a diabetic that receives insulin) should also be documented. Potential exposure to toxins (insecticides, prescription medications, herbicides) and the possibility of trauma should be determined.[107] Signalment, when coupled with the history and physical and neurological examination findings, may also provide insight into the potential etiologies of SE. For example, dogs with genetic epilepsy typically experience their first seizure between 6 months and 6 years of age. A recent study demonstrated that cats with an onset of seizures after the age of 7 years were 3.5 times more likely to have structural-metabolic epilepsy than unknown/idiopathic epilepsy.[108]

Physical examination findings

Most commonly, dogs in SE will present with generalized CSE. With prolonged seizure activity, cerebral autoregulation may fail.[107] In this instance, the patient may present with a depressed level of consciousness with only occasional muscle twitching. In patients with markedly depressed consciousness, the small animal coma scale score can be used to assess the neurological status of the patient (Figure 1).[107] A depressed level of

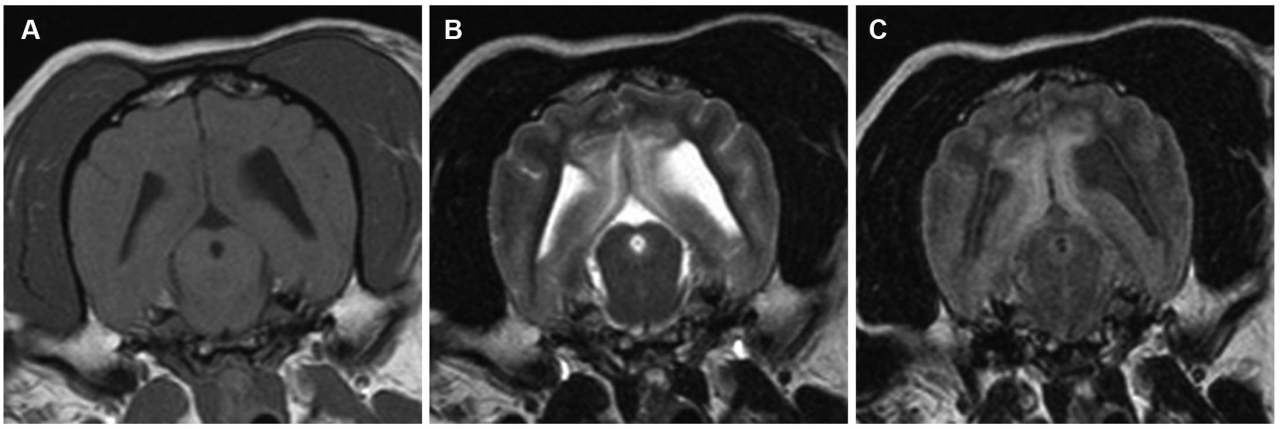

Figure 2: Transient MR abnormalities induced by SE in a dog.

consciousness can be a postictal manifestation, a consequence of underlying structural or metabolic brain disease, due to cytotoxic edema from prolonged seizure activity, or may represent NCSE, though NCSE can only be confirmed with EEG. Other physical examination abnormalities may include hyperthermia, superficial abrasions, ptyalism, altered mentation, pulmonary crackles, urination, defecation, and vocalization. Patients that have experienced trauma may have other physical examination evidence of such. Patients experiencing SE may have neurologic deficits observed prior to or after termination of seizure activity. Neurologic deficits may be caused by the underlying disease process, anti-epileptic drugs used to treat SE, transient ictal-induced changes in the brain, or the postictal state. The clinician's index of suspicion for structural-metabolic epilepsy should be raised in animals that display persistent, focal, interictal neurological deficits for ≥48 hours following cessation of seizure activity.

Diagnostic minimum database

The authors' recommended diagnostic minimum database for patients with SE (Figure 1) consists of a battery of bedside and more comprehensive laboratory tests that are intended to be complementary to the results of history and physical examinations. This approach provides the clinician with a baseline evaluation of vital parameters and systemic homeostasis, allows for targeted resuscitative therapies, screens for underlying metabolic disorders that may have precipitated SE, and aids in the identification of any significant comorbidities or complications of SE. Additional diagnostic tests such as anti-epileptic drug therapeutic monitoring, evaluation for specific underlying conditions such as portosystemic shunt or insulinoma, and diagnostic imaging examinations of the brain should be tailored to the individual.

Electroencephalography

In patients that present with generalized CSE, the diagnosis can usually be made based solely on clinical criteria. Performance of EEG to evaluate for ictal discharges and NCSE is indicated in those patients that have historical evidence of potential seizure activity but are not overtly convulsing upon presentation. The EEG may also be helpful to discriminate nonepileptic paroxysmal disorders, such as cardiogenic syncope or movement disorders, from epileptic seizures.[109] The use of continuous EEG monitoring in the management of SE will be discussed in the companion article to this review.

Diagnostic imaging of the brain and cerebrospinal fluid analyses

MRI is the preferred modality to image the brain. In patients with SE, the primary indication for MRI and CSF examinations is to identify any underlying structural brain disease. Reversible MRI abnormalities have been documented in dogs as a consequence of seizure activity.[56] As these lesions are postulated to represent vasogenic and cytotoxic edema, they often appear as bilaterally symmetrical T1-hypointense and T2-hyperintense lesions with a predilection for the temporal and pyriform lobes, although they may also be observed in the cingulate gyrus and hippocampus (Figure 2).[56] If seizure activity can be abolished, these lesions will improve or resolve in many patients over a period of 1–18 weeks.[56] Seizure activity has also been shown to induce alterations in CSF total nucleated cell counts in dogs, with nucleated cell counts tending to decrease as the temporal duration between the last seizure and CSF collection increases.[110]

Diagnostic imaging of the brain and CSF analysis are not usually necessary for the diagnosis of metabolic and toxic encephalopathies, although MRI abnormalities associated with inborn errors of metabolism, global brain ischemia, hepatic encephalopathy, and hypertensive

encephalopathy have been described.[111] In systemically stable patients, MRI and CSF analysis may be indicated in the comprehensive evaluation of patients with suspected idiopathic/genetic epilepsy.

Summary

Status epilepticus is a common emergency that may lead to numerous adverse neurologic and systemic consequences, and that can be precipitated by a variety of conditions. The pathophysiologic basis of SE is complex and involves failure of the mechanisms that normally stop seizure initiation. Generalized CSE is currently the predominant clinical presentation of SE in dogs and cats. However, NCSE has been recognized in veterinary medicine, and represents a diagnostic challenge to the clinician since it can only be confirmed with EEG. Medical history, physical examination, and initial diagnostic battery help the clinician to optimize emergency patient care, identify and treat complications of SE, and hone the rule out list for the patient with status epilepticus.

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