Seizures: Who, What, and Why?

University of Illinois Fall Conference
Kari D. Foss, DVM, MS, DACVIM (Neurology)
University of Illinois, Urbana, IL

OBJECTIVES OF THE PRESENTATION

- To review the most up-to-date terminology in regard to epilepsy and the pathophysiology and classification of seizure disorders
- To discuss the recommendations on when to start antiepileptic therapy

KEY POINTS

Seizures are the most common neurologic problems in small animal medicine with an estimated prevalence of 0.6-0.75% in the general population. Idiopathic epilepsy is between 0.5-5% of the pet population. Therefore, understanding the underlying causes of seizures and how to diagnose these patients becomes important in discussing the overall prognosis and expectations with clients.

OVERVIEW

Terminology

1. Seizure – any sudden, short lasting and transient event. Does not imply event is epileptic.
2. Epileptic seizure – manifestation of excessive synchronous activity in the brain due to abnormal excessive and/or synchronous epileptic neuronal activity
    a. Results in transient occurrence of signs which may be characterized by short episodes of convulsions or focal motor, autonomic, or behavioral features.
3. Epilepsy – having at least two unprovoked epileptic seizures >24 hours apart
4. Cluster seizures – two or more epileptic seizures within a 24-hour period. Regain consciousness in between seizures.
5. Status epilepticus – greater than five minutes of continuous seizure activity OR two or more discrete seizures without full recovery of consciousness
6. Reactive seizures – occur as a natural response from the normal brain to a transient disturbance in function (metabolic or toxic in nature)
    a. Reversible/cease when condition resolved

Seizure Classification

1. Seizure type
    a. Generalized epileptic seizures – bilateral involvement of cerebral hemispheres. Generally, patients will lose consciousness as well as have salivation, urination, and/or defecation
        i. Tonic-clonic – first part of the seizure is the tonic phase with sustained contraction of all muscles and falls to side. There is also salivation, urination, or defecation. The tonic phase is about 1 minute or so before

clonic phase begins, consisting of paddling or rhythmic jerking of limbs and chewing movements. The clonic phase is variable in duration

ii. Tonic – only generalized muscle rigidity; no clonic phase
iii. Clonic – paddling and jerking; no tonic phase
iv. Myoclonic – brief, shock like contractions and may be generalized to confined to a specific muscle group
*Not all myoclonic jerks are epileptic
v. Atonic – Sudden, brief losses of muscle tone
vi. Absence – Defined as brief, losses of consciousness in people and requires diagnosis with EEG. Rare in veterinary medicine.

b. Focal epileptic seizures – characterized by lateralized or regional motor signs indicating abnormal activity in one region of a cerebral hemisphere
i. Motor – rhythmic contractions of facial or masticatory muscles, abnormal movements of one limb, turning head to one side
ii. Autonomic – parasympathetic and epigastric signs (hypersalivation, vomiting, dilated pupils)
iii. Behavioral – sensory symptoms such as anxiousness, unprovoked aggression, "fly-biting", impaired consciousness, restlessness

2. Etiology
a. Idiopathic – most common cause of epilepsy in dogs. Several consistent features in dogs:
i. Age of onset usually between 1-5 years of age; may see < 1 year but if < 6 months, may want to consider other causes.
ii. Inherited in several breeds (see box)

Box 1. Breeds predisposed to idiopathic epileptic seizures

Australian Shepherd*
Beagle
Belgian Shepherd
Begian Tervuren
Bernese Mountain dog
Border Collie*
British Alastian
Dachshund
English Springer Spaniel
Finnish Spitz
German Shepherd dog*
Golden Retriever
Greater Swiss Mountain dog
Irish Wolfhound
Italian Spinoni*
Keeshond
Labrador Retriever
Lagatto Romagnolo
Petit Briquet Griffon Vendéen
Shetland Sheepdog
Standard Poodle
Vizsla

*Breeds known to have moderate to severe courses of idiopathic epilepsy

iii. Most commonly present as generalized tonic-clonic or focal with secondary generalization
iv. Occur spontaneously and more commonly at night or when the patient is resting or sleeping
v. May be elicited by a stimulus – loud noise, visits to the veterinary clinic or groomer
vi. Sub-classified into three sub-groups
1. Idiopathic epilepsy (genetic) - causative gene identified
2. Idiopathic epilepsy (suspected genetic) – genetic influence supported by high breed prevalence, genealogical analysis, and/or familial accumulation of epileptic individuals
3. Idiopathic epilepsy (epilepsy of unknown cause) – epilepsy in which the nature of the underlying cause is as yet unknown with no indication of structural epilepsy

b. Structural epilepsy – recurrent seizures caused by an identifiable lesion or other specific etiology
i. Degenerative
ii. Anomalous
iii. Neoplastic
iv. Inflammatory
v. Infectious
vi. Trauma
vii. Vascular

Phases of epileptic seizures

1. Preictal – long-term indication of a forthcoming seizure
a. Patient my exhibit abnormal behavior such as restlessness, clinging to the client, vocalizing
b. Not always recognized in veterinary medicine
c. Not to be confused with focal seizures, which are brief events
2. Ictus – actual seizure activity
3. Postictal – transient abnormalities in brain function that become apparent after the ictal signs have ended.
a. May see restlessness, ataxia, blindness, deafness, disorientation
b. Typically resolve after several minutes but may last for days

Diagnostic evaluation

1. Differential Diagnoses – It is important to first determine if the events are epileptic seizures versus a different episodic paroxysmal disorder
a. Seizures have spontaneous onset, stereotypic signs, self-limiting time course
b. Exclude other imitators:

Table 1 Clinical characteristics of episodic disorders

Discriminator	Syncope	Narcolepsy/ Cataplexy	Neuromuscular weakness	Paroxysmal behaviour changes (compulsive disorder)	Vestibular attack	Paroxysmal Dyskinesia	Idiopathic head tremor	Seizure
Clinical status between episodes	Normal or arrhythmia, pulse deficits, heart murmur, cyanosis, abnormal lung auscultation	Altered sleep/wake cycle, normal clinical examination	Normal or generalised weakness, muscle atrophy, pain, decreased reflexes	Normal	Normal	Normal	Normal	Normal or forebrain signs
Precipitating event or trigger	Exercise, excitement	Excitement, eating	Activity, exercise	Behavioural triggers (*e.g.,* fear)	None	None or activity, exercise, excitement, stress	None or stress, fatigue, overstimulation	None or flashing lights, anxiety, stress
Pre-event changes	None	None	None	None	None	None	None	Pre-ictal signs may be observed including: anxiety, restlessness, increased affection, contact-seeking, withdrawal, hiding, aggressiveness, and vocalization
Event description	Brief, sudden collapse and rapid recovery	Sudden collapse	Stiff, stilted gait prior to collapse	Pacing, barking, licking, chasing imaginary objects or tail, chewing objects	Head tilt, nystagmus, vestibular ataxia, collapse towards side of head tilt	Dystonia, chorea, ballismus, athetosis, tremors, impaired posture, inability to stand or walk	Vertical or horizontal rhythmic head movement	Depending on seizure focus, focal or generalized, tonic-clonic movements most common
Level of consciousness	Reduced to absent	Normal if only cataplexy. Absent (asleep) in narcolepsy	Normal	Normal	Normal or disorientated	Normal	Normal	Often impaired
Autonomic signs	Possible abnormalities of heart rate and rhythm	None	None	None	None	None	None	Possible: hypersalivation, defaecation, urination
Muscle tone	Flaccid (all body)	Flaccid (all body)	Often flaccid (can appear spastic with certain myopathies)	Normal	Unilateral decrease in extensor muscle tone	Hypertonicity (focal or generalised)	Normal	Typically increased: tonic (hypertonicity) or alternating tonic-clonic movements
Lateralising signs	No	No	No	No	Yes	Possible	No	Possible
Duration	Seconds	Seconds to minutes	Minutes to hours	Minutes to hours	Seconds to hours	Seconds to hours	Seconds to hours	Seconds to minutes or > 5 min in case of status epilepticus
Post-episodic changes	None	None	None	None	None	None or tiredness	None, tiredness, or restlessness	Post-ictal signs frequently occur including: disorientation, aggressive behaviour, restlessness, pacing, lethargy, deep sleep, hunger, thirst, ataxia, proprioceptive deficits, and blindness
Further comments	May be accompanied by cough, increased respiratory noise	Often occurs in young purebred dogs.	May be accompanied by dysphagia, dysphonia, regurgitation, dyspnoea	History of anxiety disorder	Subtle signs of vestibular disease might persist	Interaction with the owner can alleviate or interrupt the episode. Consider breed specific disorders and age at onset.	Episodes can be interrupted by the owner	Facial muscles often involved during the ictus

De Risio et al. International veterinary epilepsy task force consensus proposal: diagnostic approach to epilepsy in dogs. BMC Vet Res. 2015 Aug 28;11:148.

2. Detailed and accurate history
    a. Description of the event/seizures including frequency and duration, in addition to other focal signs at the start.
    b. Obtain a video if possible
    c. Do the events occur at a certain time of day or are they associated with specific situations?
    d. Familial history of seizures, illness, injuries, vaccination status, diet, toxin exposure as well as any inter-ictal changes

3. Complete physical and neurologic examination
    a. Detection of any persistent neurologic deficits – may see temporary post-ictal changes
    b. Identify abnormalities suggestive of underlying disease processes (cardiac disease, etc.)
    c. Minimum database – complete blood count, serum chemistry profile paired
        i. Additional labwork may include serum bile acids, blood lead levels, thyroid panel
4. Ancillary testing
    a. CSF and MRI indicated in patients with persistent inter-ictal neurologic deficits, refractory seizures, age of onset of either < 1 year or > 5 years.
    b. Always indicated in cats due to the low incidence of idiopathic epilepsy in this species.
    c. EEG may be helpful in determining if events are epileptic seizures or nonepileptic events.

<u>When to treat</u>

The ideal goal of antiepileptic drug (AED) therapy is to find a balance in control of the seizures with the patient and client's quality of life. When deciding to start, consider the general health of the patient as well as the client's lifestyle, financial limitations, and comfort with treatment plan.

In people, there are a number of relative risk factors that have been identified including current or previously defined lesions or trauma, presence of inter-ictal EEG epileptic discharges, and a history of marked post-ictal adverse effects. The decision to treat is a based on the goals of decreasing or eliminating epileptic events, decrease seizure activity, avoid adverse effects, and decrease seizure-related mortality and morbidity.

At this time, there is no similar information available in the canine population. There is strong evidence in people to support there is no benefit to starting therapy after a single event; however, evidence does support that earlier intervention is correlated with a better outcome for seizure control.

The ACVIM Small Animal Consensus Statement on Seizure Management in Dogs (2015) recommends the use of the following as guidelines on starting AED treatment:

1) Identifiable structural lesion present or prior history of brain disease or injury
2) Acute repetitive seizures or, status epilepticus
3) Two or more seizure events within a 6-month period
4) Prolonged, severe, or unusual postictal periods

SUMMARY

It is important to always obtain a detailed history and to perform a thorough neurologic examination, which help further classify the suspected classification of seizure activity. Understanding the underlying causes of epileptic seizures in patients will provide valuable information in regard to recommending diagnostics as well as when to begin AED therapy.

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