NEUROLOGY

How to Diagnose and Manage Feline Seizures

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Abstract

Seizures are common in cats. However, recognition of seizures can be challenging given the variety of clinical presentations. Obtaining a detailed history is an important diagnostic step. Systemic evaluation for extracranial causes of seizures should be performed prior to exploring intracranial causes. Detailed seizure logs are important for monitoring and adjusting antiseizure therapy. Phenobarbital, zonisamide, and levetiracetam are appropriate maintenance choices for feline seizure management. Quality of life for both the cat and owner is important to consider when starting antiseizure therapy.

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Take-Home Points

- Seizures in cats can be challenging for clinicians to identify and manage due to the wide range of clinical signs and lack of studies evaluating the safety and efficacy of antiseizure drugs (ASDs).
- Structural or metabolic seizures are more common than idiopathic epilepsy in cats.
- Feline seizures often manifest as partial with or without secondary generalization and include hypersalivation, mydriasis, running fits, facial twitching, aggression, and autonomic signs.
- Phenobarbital, levetiracetam, and zonisamide are acceptable maintenance ASD choices.
- Potassium bromide and diazepam are not recommended in cats due to the severity of their adverse effects.
- Quality of life is important to consider when starting ASDs in cats.

Seizures are transient disturbances in forebrain function secondary to imbalances in excitatory and inhibitory neural transmission.[1] Epilepsy, or recurrent seizures, is a common neurologic condition of cats.[2-4] Feline epileptic seizures can be a challenge for clinicians due to the wide variety of clinical signs and lack of studies evaluating the efficacy and safety of antiseizure drugs (ASDs) in cats.

Etiology

Seizures in cats can be classified as idiopathic (no underlying brain lesion present), structural (seizures secondary to an underlying brain lesion), or metabolic (seizures secondary to a metabolic or toxic cause).[5] Further subcategories of structural and metabolic seizures are listed in **TABLE 1**. Seizures that are structural or metabolic are more common than idiopathic epilepsy in cats.[6]

Status epilepticus, altered interictal neurologic state, and seizure onset after the age of 7 years have been demonstrated more frequently in structural epilepsy than idiopathic epilepsy.[6] Additionally, cats that develop seizures at less than 12 months of age are more likely to have structural epilepsy than idiopathic epilepsy.[7]

Clinical Manifestation

Seizures have 4 characteristic stages: prodrome, aura, ictus, and postictus.[5] The prodrome precedes the onset of the seizure and can include restless or anxious behavior. The aura, a subjective feeling preceding the ictal event, cannot be differentiated from the prodromal stage in cats without use of electroencephalography (EEG). These 2 stages are classically referred to as the "preictal" stage.

The ictus is the seizure event itself. Recognizing feline seizures can be challenging given their diverse clinical presentation and subtle signs.[7-9] Partial seizures are isolated to specific parts of the body, whereas generalized seizures affect the entire body. The term "partial seizure" is used to describe the clinical manifestation, while "focal seizure" is an EEG term. Seizures in cats often manifest as partial seizures with or without secondary generalization. This manifestation of seizures can be extremely variable between cats and frequently involves excessive salivation/drooling, mydriasis, running fits, aggression, facial twitching, and urination (**VIDEO 1**).[5]

VIDEO 1
Scan the QR code to see a feline seizure characterized by mydriatic pupils, hypersalivation, and twitching.

TABLE 1 Diagnostic Differentials for Structural and Metabolic Seizures in Cats[3]

EPILEPSY TYPE	DIFFERENTIALS
Structural	
Vascular	▪ Hypertension ▪ Feline ischemic encephalopathy ▪ Coagulopathy ▪ Polycythemia ▪ Thromboembolic disease

Inflammatory/infectious	▪ Toxoplasmosis
	▪ Cryptococcosis
	▪ Blastomycosis
	▪ Feline infectious peritonitis
	▪ Feline leukemia virus
	▪ Feline immunodeficiency virus
	▪ Rabies
	▪ Aberrant parasitic migration
	  ▪ Dirofilariasis
	  ▪ Cuterebriasis
	▪ Meningoencephalitis of unknown etiology

Traumatic	▪ Traumatic brain injury
Anomalous	▪ Hydrocephalus ▪ Lissencephaly
Neoplastic	▪ Meningioma ▪ Lymphoma ▪ Glioma ▪ Pituitary neoplasm ▪ Choroid plexus tumor ▪ Ependymoma ▪ Nasal adenocarcinoma ▪ With extension into the brain ▪ Metastatic neoplasm
Degenerative	▪ Feline hippocampal necrosis ▪ Storage disease
Metabolic	
Metabolic	▪ Thiamine deficiency ▪ Hyperthyroidism ▪ Hepatic encephalopathy ▪ Renal encephalopathy/uremia ▪ Hypoglycemia ▪ Hypocalcemia ▪ Sepsis ▪ Rapid correction of hypernatremia
Toxic	▪ Pyrethroids ▪ Organophosphate ▪ Lead ▪ Ethylene glycol

The postictal stage can include ataxia, blindness, deafness, aggression, and excessive hunger/thirst.[5] This stage can give indications as to whether the event was a true seizure.

Diagnostic Workup

A detailed history is a crucial first step in the management of feline seizures. Important points to discuss include the details of the preictal (what the cat was doing before the seizure), ictal (what the cat was doing during the seizure), and postictal (what the cat was doing after the seizure) stages; the length of the

RESOURCE 1
Scan the QR code to access a feline seizure history collection form that can be used in the clinic.

seizure; when the event occurred; any events prior to the seizure (such as stressful events); and the presence of autonomic signs (**RESOURCE 1**). Videos of the event can be valuable for identifying true seizures.

Following a thorough history, complete physical and neurologic assessments should be undertaken. An abnormal interictal neurologic examination is more likely to be indicative of structural epilepsy. However, a normal examination does not rule out an underlying structural cause.[6,7]

Prior to pursuing advanced neurologic diagnostics, extracranial causes of seizures must be ruled out. Diagnostic tests may include CBC, serum chemistry, blood pressure measurement, and urinalysis. Feline leukemia virus, feline immunodeficiency virus, and thyroid testing may be considered as indicated. Bile acids may be helpful in evaluating for underlying hepatic encephalopathy. Ammonia testing will likely not be helpful, as cats can demonstrate a postictal hyperammonemia without underlying hepatic pathology.[10]

Once extracranial causes have been ruled out, brain magnetic resonance imaging with or without cerebrospinal fluid tap can be considered. For subtle or nonconvulsive signs of seizures, diagnosis of seizure may require EEG confirmation.[8,11]

Antiseizure Drugs

Treatment of seizures is different in cats than in dogs. Therefore, safety profile and efficacy must be considered prior to choosing an ASD for feline patients.[3,12] Furthermore, owners must be committed to frequent drug administration, managing potential adverse effects, the cost of monitoring, and the potential need for lifelong administration. Repeat oral administration of ASDs can be challenging for owners and can result in poor adherence and seizure control.

It is important to emphasize the goals of seizure management with owners: reduction in seizure frequency and severity while avoiding adverse effects.[13] An ASD is considered effective when it results in a reduction of seizure frequency/severity by approximately 50% or more.[14] Owners should be advised to keep a detailed seizure log to better determine whether ASDs are indicated and, if so, when adjustments should be made. ASD therapy must be tailored to each individual patient.

Starting maintenance therapy in cats is indicated for patients with seizures that occur more than once every 12 to 16 weeks (in the case of primary epilepsy), cluster seizures (more than 1 seizure in a 24-hour period), status epilepticus (seizure lasting longer than 5 minutes), or any seizures secondary to structural epilepsy.[13] If an ASD is considered ineffective (i.e., increasing seizure frequency/severity despite appropriate administration or minimal to no reduction in seizure frequency), the treatment plan must be reevaluated. Therapeutic serum levels, in the case of phenobarbital, should be checked to ensure appropriate therapeutic levels. If the maximum dose has been reached on a single ASD, the addition of another ASD should be considered.

Phenobarbital

Phenobarbital is among the most commonly used ASDs in cats and is considered a first-line therapy.[12,15] Phenobarbital is a long-acting barbiturate that depresses the central nervous system and exhibits γ-aminobutyric acid (GABA)–like effects.[16] The starting maintenance dose is 2.5 to 5 mg/kg PO q12h.[13,17] At the authors' institution, 8.1 mg/cat PO q12h (1/2 of a 16.2-mg tablet) is utilized as a starting dose. In an emergent situation, phenobarbital may be loaded initially (8 to 16 mg/kg IV once) prior to starting maintenance. Sedation can be expected but is temporary. Once-daily oral treatment of phenobarbital has been evaluated retrospectively with satisfactory seizure control at a mean oral dose of 2.6 mg/kg PO q24h; however, larger prospective studies are needed.[18] Transcutaneous phenobarbital has been described; however, achieved serum levels are subtherapeutic.[19]

Phenobarbital is metabolized via the liver (cytochrome P450).[16] Phenobarbital reaches steady state 2 weeks after starting the medication; therefore, serum

phenobarbital levels must be checked at this time. The serum level guides further dose adjustments. Phenobarbital levels must be checked 2 weeks after changing the dose or every 6 to 12 months thereafter. The therapeutic serum concentration for phenobarbital is 20 to 35 µg/mL.[5] Additionally, complete blood analysis, including serum chemistry and CBC, should be performed every 6 to 12 months.

In dogs, phenobarbital is known to cause serum liver enzyme induction and hepatotoxicity. Hepatic enzyme induction or other biochemical abnormalities are not seen in cats receiving phenobarbital.[20,21] This further strengthens the safety profile of phenobarbital use in cats. The most commonly reported dose-dependent adverse events in cats treated with phenobarbital include sedation, ataxia, polyuria, polydipsia, polyphagia, weight loss, and behavioral changes.[12,21] Reported idiosyncratic drug reactions include lymphadenopathy, pseudolymphoma, skin eruptions, pyrexia, and coagulopathies.[12,22,23] Blood cytopenias may occur in cats treated with chronic phenobarbital therapy; however, clinical signs are typically mild to moderate.[21,24]

Zonisamide

Although phenobarbital is a safe and effective ASD for most cats, some cats may have inadequate seizure control with phenobarbital alone or not tolerate phenobarbital.[12,25] Zonisamide is an ASD approved for treatment of focal seizures in human adults and has been effective in animal models.[24,25] Zonisamide inhibits voltage-gated sodium and T-type calcium channels; it also has neuromodulatory effects facilitating inhibitory neurotransmission.[16]

Reported doses of zonisamide vary in the veterinary literature, with a maintenance dose of 5 to 10 mg/kg PO q12h to q24h reported.[5,25,26] Twice-daily dosing may be more effective in cats; however, once-daily dosing appears to be well tolerated given the extended half-life of zonisamide in cats.[25] Zonisamide is metabolized via the liver (cytochrome P450). Complete blood analysis, including serum chemistry and CBC, should be performed every 6 to 12 months. Therapeutic serum levels have not been determined for dogs or cats, and monitoring serum levels is controversial.

Reported adverse events associated with zonisamide may include sedation, ataxia, anorexia, vomiting, and diarrhea.[25-27] There is a single case report of suspected zonisamide-related anticonvulsant hypersensitivity syndrome in a cat, characterized by lymphadenopathy, hyperglobulinemia, and cytopenia.[28]

Levetiracetam

Levetiracetam is a popular ASD in veterinary medicine due to its lack of systemic adverse effects.[29] There are few studies of its use in cats; however, there is specific known efficacy with audiogenic reflex seizures.[30]

Levetiracetam works through interaction with SV2A (synaptic vesicle protein 2A), modulation of voltage-gated calcium channels, and alteration of GABA turnover.[31] Traditionally, it is administered every 8 hours. However, large fluctuations in plasma drug concentration through the dosing interval can be expected, as the reported half-life of levetiracetam in the cat is only 3 hours.[32]

Levetiracetam appears to be well tolerated in cats and may be beneficial as an adjunct therapy.[33] The reported dose is 20 to 25 mg/kg PO q8h but can be increased.[30,32,33] Liquid formulations are also available. In an emergent situation, a higher dose may be administered initially (60 mg/kg IV once) prior to starting maintenance therapy.

Given the difficulty of administering an ASD to a cat 3 times per day, once-daily dosing has been evaluated.[34,35] Administration of a single 500-mg extended-release caplet per cat (> 5 kg [11 lb]) every 24 hours may provide an easier alternative to dosing 3 times daily; however, the size of the caplet limits the ease of administration, and individual variation can be expected.[35]

Monitoring levetiracetam levels and complete blood analysis are not often performed due to the lack of systemic adverse effects. Reported adverse events can include lethargy, ataxia, hypersalivation, and inappetence, which are often transient and mild.[30]

Antiseizure Drugs to Avoid

Potassium bromide is not recommended for use in cats, as the incidence of adverse effects outweighs its

benefits. Specifically, potassium bromide has been linked with the development of eosinophilic bronchitis in cats that can be life threatening.[36-38]

Diazepam is not an appropriate ASD choice in feline patients due to inadequate evidence supporting its efficacy and the possibility of severe and potentially life-threatening adverse events, including fulminant hepatic necrosis and liver failure.[12,39,40]

Long-Term Quality of Life

A diagnosis of epilepsy can affect quality of life for both the cat and the owner.[41] Owners may suffer from a heightened burden of care due to the emotional and financial commitment associated with the diagnosis. Factors impacting burden of care for owners and quality of life for cats were evaluated in 1 study to help provide effective solutions and adequate support in management.[42] This study showed that quality of life was significantly higher in cats with controlled seizures, epilepsy onset before the age of 5 years, and no adverse effects of treatment. Additionally, the burden of care was significantly lower in owners who felt supported by their veterinarians, emphasizing the importance of open communication with owners of epileptic cats.[42]

Summary

Epilepsy is a common neurologic condition in cats. However, recognition of seizures can be challenging given the wide variety of clinical presentations. Structural or metabolic seizures are more common in cats than primary epilepsy. Feline seizures often manifest as focal with or without secondary generalization and involve hypersalivation, mydriasis, facial twitching, aggression, autonomic signs, or running fits. Obtaining a detailed history is an important diagnostic step, and detailed seizure logs are important for monitoring and adjusting antiseizure therapy. Phenobarbital, zonisamide, and levetiracetam are appropriate maintenance choices; potassium bromide and diazepam are not. When starting antiseizure therapy, it is important to consider quality of life for both the cat and the owner. TVP

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CE Quiz Questions

1. **Which of the following antiseizure drugs has been linked with eosinophilic bronchitis in cats?**
   a. Phenobarbital
   b. Potassium bromide
   c. Levetiracetam
   d. Zonisamide

2. **Which of the following is not an indication to start antiseizure therapy?**
   a. Seizures secondary to structural causes
   b. Cluster seizures
   c. Status epilepticus
   d. First-time seizure with no overt structural cause

3. **Serum phenobarbital levels should be checked _____ after changing the phenobarbital dose.**
   a. 1 day
   b. 1 week
   c. 2 weeks
   d. 3 months

4. **Which of the following antiseizure drugs has a reported half-life of 3 hours in cats?**
   a. Zonisamide
   b. Levetiracetam
   c. Phenobarbital
   d. Diazepam

5. **Which of the following statements is false?**
   a. Idiopathic epilepsy is more common than structural or metabolic epilepsy in cats.
   b. Diazepam is an inappropriate antiseizure drug due to the risk of severe adverse events including fulminant hepatic necrosis and liver failure.
   c. Maintaining a seizure log is important for adjusting antiseizure drug therapy.
   d. The therapeutic serum level for phenobarbital is 20 to 35 µg/mL.

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