Seizures in Cats—How to Investigate

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Generalized-onset seizures have been reported as the most common type of seizure in cats. However, the studies which have documented this, used events described by the cat owners in the vast majority of cases and therefore focal clinical manifestations at the onset of the ictus may have gone unnoticed. Only two studies have reported higher prevalence of focal-onset seizures to generalized-onset seizures in cats with various seizure etiologies. Secondary generalization occurred in 65% and 90% of these cats, respectively.

Focal Seizures

Focal seizures (previously known as partial seizures) originate from abnormal activity in one region of a cerebral hemisphere, resulting in asymmetric signs initially. Motor manifestations of a focal seizure may include abnormal movements (automatisms) such as turning of the head to one side, rhythmic contractions of a limb or facial muscles, ear and/or whisker twitching, lip smacking or chewing movements. Circling, rapid running or climbing activity are also common in cats with focal seizures and may suggest temporal lobe involvement. Tail chasing, limb chewing and fly biting are focal seizure manifestations that are presumed to result from abnormal sensory experiences such as tingling, pain or visual hallucinations. Less commonly, focal seizures cause strictly autonomic signs, with episodes of vomiting, drooling, diarrhea and apparent abdominal discomfort, or rhythmic pupillary dilation and constriction (hippus). Complex focal seizures (formerly called psychomotor seizures) are focal seizures with altered mentation, resulting in excessive vocalization, growling, head pressing, pacing, aimless walking and occasionally unprovoked aggression or extreme fearfulness. Some cats with complex focal seizures will be described by owners as acting as if they are ‘possessed’ or in a trance during the seizure, while others may be severely obtunded and non-responsive. Focal seizures sometimes progress into a generalized tonic-clonic seizure and the secondary spread can be so rapid that the initial focal component is missed and the seizure is misclassified as a generalized-onset seizure.

Reflex Seizures

Reflex seizures are seizures that can be consistently provoked by specific stimuli or events. The most common precipitating factor in people is a flickering light, but certain sounds and eating have also been identified as triggers. Reflex seizures in humans may occur with any seizure etiology and are reported to be generalized or focal, with myoclonic jerks being most common.

Seizures that were consistently provoked by specific high-pitched sound stimuli have been described in 96 cats, characterizing a disorder called feline audiogenic reflex seizures. The sounds that served as triggers for the seizures were varied and included paper or plastic bag crinkling, the clinking of coins or keys and the clicking of an owner's tongue. All cats developed generalized tonic-clonic seizures and 94% also developed myoclonic jerks with the noise stimulus. No underlying cause for the seizures could be identified with metabolic and intracranial evaluation. Neurologic examinations between seizures were normal, except that 50% of the cats were hearing impaired or deaf and 21% were visually impaired. Cats ranged from 10 to 19 years of age at the onset of their seizures (median age 15 years) and a degenerative brain condition was suspected. Birman cats were over-represented. In treatment trials, levetiracetam was more successful than phenobarbital at controlling both the generalized tonic-clonic seizures (69% vs 27%) and the myoclonic seizures (93% vs 7%).

ETIOLOGY

Seizure type does not seem to be predictive of underlying seizure etiology. No association has been identified between various types of seizures (focal-onset with or without secondary generalization, or generalized-onset) and different seizure etiologies (reactive, symptomatic, or idiopathic). Although the percentage of cats with generalized-onset tonic-clonic seizures appeared higher among those with idiopathic epilepsy compared to cats with other seizure etiologies, this difference was not statistically significant. Likewise, although the percentage of cats with status epilepticus appeared higher in those with reactive (6/20, 30%) or symptomatic (10/45, 22%) seizures than in those with idiopathic epilepsy (1/23, 4%), differences were not statistically significant. Age at the onset of seizures varies among studies and overall ranges from 1 week to 20 years. The age at seizure onset is significantly different between cats with idiopathic epilepsy and cats with symptomatic (structural) or reactive epilepsy. In one study, cats younger than 7 years of age were more likely to have idiopathic epilepsy and those older than 7 years of age were more likely to have symptomatic (structural) or reactive epilepsy. In another study, cats diagnosed with idiopathic epilepsy were significantly younger (mean, 3.5 years) when the first seizure occurred than cats with reactive seizures (mean, 8.2 years) or with symptomatic (structural) epilepsy (mean, 8.1 years). Age at seizure onset was not significantly different between cats with symptomatic (structural) epilepsy and cats with reactive seizures. Age at seizure onset and duration of the seizure disorder prior to examination are not significantly different between cats with symptomatic (structural) and cryptogenic epilepsy. Among cats with symptomatic (structural) epilepsy, cats with meningoencephalitis (mean age 3.4 years) are generally younger than cats with neoplasia (mean age 12.1 years). Among cats with intracranial neoplasia, cats with lymphoma (median age 5 years, mean age 5.6 years) are

significantly younger than cats with meningiomas (median age 11 years, mean age 10.3 years).

Secondary Seizures

Seizures caused by intracranial pathology (structural epilepsy, also called secondary epilepsy or symptomatic epilepsy) account for 40–70% of all recurrent seizure disorders in cats. Lesions producing seizures are located in the forebrain, most often in the cerebral cortex, but occasionally in the subcortical regions of the brain, particularly the thalamus. Approximately 75% of cats with structural epilepsy have interictal neurologic abnormalities suggesting structural disease of the forebrain, including unilateral or asymmetric menace deficits, paresis, decreases in proprioceptive placing, circling and subtle changes in personality or behavior. Lesions of the olfactory lobe, rostral frontal lobe or midline thalamus can, however, remain clinically silent for some time, other than causing seizures. It was recently reported that 23% of cats older than 6 years at seizure onset with a normal inter-ictal neurologic examination had a significant structural abnormality on MRI causing their seizure disorder. Another recent study looked to identify seizure etiologic classification for cats that developed seizures at <12 months of age and describe the long-term outcome of affected cats. Seven of the 15 cats in the study had structural epilepsy, 4 had idiopathic epilepsy, and 4 had reactive seizures. Median age at seizure onset was 27 weeks (range, 0.4 to 41 weeks). Cluster seizures were reported in 6 cats, and status epilepticus was reported in 2. Age at the onset of seizures, presence of cluster seizures, and seizure semiology (i.e., generalized vs. focal seizures) were not significantly associated with seizure etiologic classification. Results suggested that cats that developed seizures at <12 months of age were more likely to have structural epilepsy than idiopathic epilepsy or reactive seizures. Therefore, advanced diagnostic imaging is recommended in cats with juvenile-onset seizures if metabolic and toxic causes are excluded.

The most common causes of structural epilepsy in cats include neoplasia, inflammatory disorders, and vascular disorders such as infarcts or hemorrhage. Congenital anomalies, degenerative disorders, storage diseases and thiamine deficiency have also been reported. Hippocampal necrosis may additionally be an important cause of recurrent seizures in cats. In most cats with an intracranial cause for their seizures, MRI and potentially cerebrospinal fluid (CSF) collection and analysis will be needed to reach a diagnosis. Medical management of seizures may be recommended while attempting to treat the underlying disease process or whenever the structural disease that is identified cannot be treated.

Feline hippocampal necrosis (FHN) is a severe structural abnormality in the brain that has been associated with seizures in cats. It is uncertain whether this hippocampal pathology

serves as an epileptogenic focus to cause seizures or if the FHN occurs secondarily to severe seizure activity. Hippocampal neurons are very sensitive to hypoxia, hypoglycemia, hyperglycemia and glutamate excitotoxicity, potentially leading to ischemic injury and necrosis following severe seizures. Hippocampal necrosis occurs in 6–30% of seizing cats and is most prevalent in cats with severe seizure disorders that have had at least one observed episode of cluster seizures or status epilepticus. Cats with focal onset seizures with secondary generalization that develop status epilepticus after a prolonged history of recurrent seizures may be at highest risk. Many epileptic cats with FHN have no other structural brain disease identified, suggesting either that the FHN is causing their seizures or that they have idiopathic epilepsy and secondary hippocampal ischemia and necrosis. In one large study evaluating 93 cats with epilepsy, the risk of FHN was highest in cats with inflammatory or neoplastic causes for their severe seizure disorder, and all cats with bilateral FHN had neoplastic or inflammatory infiltrates invading both hippocampi. Most cats with FHN are presented because of a rapidly progressive acute cluster of generalized or complex focal seizures together with interictal abnormalities, suggesting a forebrain lesion. Complex focal seizures with orofacial involvement are most common, including salivation, facial twitching, lip smacking, chewing, licking and swallowing. Behavior changes that persist between seizures often include staring into space, disorientation, aggression, rapid running, hyperexcitability and fearfulness.

Reactive Seizures

A retrospective study of nearly 800 cats referred for epileptic seizure evaluation looked to determine common causes for reactive seizures (RS) in cats. Reactive seizures were diagnosed in 62 (7.9%) of cats. The most common cause of RS was presumptive or confirmed intoxication (n=34/62; 54.8%). Toxins included permethrin (n=5/62; 8.1%), fipronil (n=1/62; 1.6%), and pesticide (n=1/62; 1.6%). Other common causes were hepatic and renal encephalopathy (n=6/62; 9.7% each), hypertension (n=5/62; 8.1%), hyperthyroidism (n=3/62; 4.8%), hypoglycemia (n=3/62; 4.8%), and hyperglycemia (n=1/62; 1.6%). Most commonly, cats with RS presented with generalized tonic-clonic seizures (n=25/62; 40.3%). A single status epilepticus was observed in 9.7% (n=6/62) and 4.8% (n=3/62) presented only with cluster seizures. Focal seizures were the only presenting sign in 3.2% (n=2/62) of cases, however in 4.8% (n=3/62) they were accompanied by tonic-clonic seizures. The mean age of all cats presented for RS was 10.8 years. In the intoxication group, the mean age was 2.9 years.

Idiopathic Epilepsy

The prevalence of idiopathic epilepsy in cats has been reported to be lower than in dogs in the few studies that have investigated prevalence of seizure/epilepsy etiology at the same institution. One study reported a prevalence of idiopathic epilepsy of 38% in cats and 48% in dogs and another study reported a prevalence of idiopathic epilepsy of 54% in cats and 68% in dogs.

The diagnosis of IE (primary epilepsy or unknown epilepsy) is one of exclusion and in dogs and cats is traditionally made based on typical signalment and seizure history, unremarkable interictal physical and neurologic examination, exclusion of underlying metabolic and toxic causes, and inability to find an intracranial cause. Historically, idiopathic epilepsy was considered to be an uncommon cause of seizures in cats. There was a perception that all cats with epilepsy must have an intracranial cause for their seizures, so when no cause could be readily found these cats were categorized as having ‘probable symptomatic’ or ‘cryptogenic’ epilepsy with no identifiable underlying cause. Cats with idiopathic epilepsy are typically younger than cats with structural epilepsy. In several studies the mean age for seizure onset in cats with idiopathic epilepsy was between 3 and 5 years, while cats with intracranial disease did not usually start experiencing seizures until they were older than 8 years of age. There are, of course, exceptions such as congenital disorders and FIP which predominantly affect young cats, while neoplasia is more common in the older cat population. Although there is considerable overlap between groups, a young adult cat is more likely to have idiopathic epilepsy than structural intracranial disease. Status epilepticus rarely occurs during the first presentation of cats with idiopathic epilepsy, but progression from a cluster of seizures to status epilepticus will occur in 10–20% of cats with idiopathic epilepsy during a lifetime (vs 40% for other seizure etiologies) and is associated with a poor prognosis for survival. Cluster seizures are common in cats with idiopathic epilepsy (53%) but their prevalence is not different from that of cats with other causes of seizures.

The 1-year survival rate for cats with reactive seizures is significantly longer than that for cats with symptomatic (structural) epilepsy. Cats with idiopathic epilepsy have a significantly longer 1-year survival rate than cats with reactive or symptomatic seizures. Cats with cryptogenic epilepsy have significantly longer survival times (mean 1.9 years) than cats with symptomatic (structural) epilepsy (<3 months). In addition, cats with status epilepticus (most commonly associated with reactive or symptomatic seizures) have a significantly shorter survival time than cats that do not have status epilepticus.

NEURODIAGNOSTIC INVESTIGATION

Historical Data

The most important component in approaching a seizure case is acquiring a thorough and accurate history. Enquiries regarding the seizure event should address a description of the event, time of day, duration and postictal effects. The purpose is to establish overall frequency, seizure type, patterns of occurrence, relationship to daily activity (e.g., exercise, sleep) and severity of post-ictal effects. It is recommended that a charting technique measuring seizure frequency and severity should be developed to aid in objective evaluation of future observed and suspected seizures.

The interictal status of the cat's cerebrocortical function (between seizures and after the postictal period) can be evaluated by asking questions concerning the animal's behavior, vision, gait and sleep/wake patterns. For example, if the cat is more withdrawn or attention seeking, showing any unusual episodes of aggression or irritability, or fails to follow simple commands, then a structural cerebral problem should be suspected. Likewise, subtle gait disturbances (stumbling up or down the stairs), visual disturbances (occasionally bumping into objects on one side) and restless sleep patterns may indicate forebrain problems.

Diagnostic Evaluation

The sequence of diagnostic testing for any animal with seizures should proceed from the least invasive to the most invasive (and expensive) diagnostic modality.

A complete blood count (CBC), biochemistry panel (including blood glucose), urinalysis and blood pressure measurement should be performed for all animals being evaluated for an epileptic seizure.

Cats <1 year of age and those being initiated on hepatic metabolized antiepileptic drug therapy should also be evaluated for hepatic disease with a serum bile acid study or resting serum NH4 concentrations.

Other individual tests for toxin exposure (e.g., plasma lead, serum cholinesterase assay), parasitic infection, or systemic illness are based on the clinical picture at the time of presentation. For cats, the basic screening should include a retroviral screen for feline leukemia and feline immunodeficiency virus and testing for serum antibodies to *Toxoplasma gondii*. Testing for the virus causing feline infectious peritonitis is not recommended, as the correlation between a positive titer and active CNS infection is low.

Due to the high incidence of symptomatic epilepsy in cats, the author recommends that advanced imaging of the brain be performed in all epileptic cats.

Cerebrospinal fluid (CSF) analysis is recommended in any animal with multifocal neurological deficits or lesions observed on MRI or CT scans. The presence of an abnormal CSF analysis has been found to be highly associated with the presence of underlying brain parenchymal lesions as detected on MR images; CSF can also be abnormal due to the seizures themselves.

Although EEG analysis is beneficial in identifying underlying epileptic foci in the cat, the overall usefulness of this test for determining diagnosis and treatment has yet to be proven. Obtaining video segments of events can be extremely helpful to clinicians to determine if an epileptic event is present. Owners should be encouraged to video an event if possible, and to try to distract the pet to determine if the event can be terminated with external stimuli. Distractibility often implies a non-epileptic event.

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