APPROACHES TO SEIZURES IN CATS

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Laurent Garosi takes us through the specifics of treating such cases, from identifying the signs and using a history effectively through to management plans

DIAGNOSIS and treatment of seizures in cats have, for a long time, been extrapolated from clinical experiences found in dogs.

It is now well-accepted that seizures in this species deserve a more specific approach. This article reviews the main particularities of clinical interest for practitioners.

Clinical features of feline seizures

An epileptic seizure is not a disease entity in itself, but a clinical sign generally indicative of a forebrain disorder. Similarly, the term epilepsy is not a specific disease, but the term used to define recurrent epileptic seizures. Consequently, a cat having a single epileptic seizure does not have epilepsy, as the seizures are not recurrent.

Seizure types can be classified into two major categories: partial and generalised. Compared to dogs, cats commonly exhibit partial seizures (Figure 1). Partial seizures are described as simple when consciousness is not impaired, or complex when consciousness is impaired. These seizures only affect part of the body and are much more difficult to recognise. They may manifest as drooling, orofacial automatism (such as eyelid or facial twitching), excessive vocalisation, growling, and abnormal head, neck or limb movement. They may progress to generalised seizures, and may occur several times throughout the day (cluster seizure).

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The focal nature of this seizure type is associated with a higher incidence of focal intracranial pathologic change in cats. Generalised seizures are usually easier to recognise than partial seizures. They are characterised by sudden collapse, loss of awareness, tonic/clonic movement of all four limbs, chewing and/or twitching of the face, and often salivation, urination and defaecation.

Prior to the actual seizure, the cat may show changes in behaviour, such as salivation, growling or pacing. Recovery from a seizure may take a few seconds to a few hours, during which the cat may appear disorientated, blind and ataxic.

Obtaining a good history

The first step is to obtain a thorough history, including the seizures' onset, frequency and description. Recognition of an epileptic seizure is essentially based on the owner's description of the event.

Apart from the unequivocal description of a generalised tonic/clonic seizure, recognition of a partial seizure can be a real challenge for the clinician. Video footage obtained by the owner can, for that particular reason, be of precious help. An epileptic seizure can be suspected based on the peracute and unexpected onset and offset, short duration (few seconds to less than five minutes), stereotypical pattern, presence of involuntary motor activity and/or abnormal mentation and behaviour, and/ or autonomic signs (salivation, urination and/or defaecation).

Ultimately, the absolute confirmation of the epileptic nature can only be obtained by simultaneously observing the physical manifestation of the seizures and characteristic electroencephalography (EEG) changes, which is rarely achievable or practical in cats.

Other paroxysmal events – such as paroxysmal movement disorder, narcolepsy/ cataplexy and syncope secondary to high-grade atrioventricular dysfunction – are rare, but should be considered as differentials. Paroxysmal movement disorders is the designation most commonly used to describe dystonic movements or postures that are not continuous but occur paroxysmally, followed by a return to normality with no neurologi cal deficit in between attacks.

Awareness is usually not impaired, and this type of paroxysmal event can last for much longer than an epileptic seizure. Narcolepsy/cataplexy is a chronic sleep disorder characterised by excessive daytime sleepiness and cataplexy (sudden loss of muscle tone in response to emotional stimuli). It is rarely reported in cats. During the event, the cat often falls into rapid eye movement (REM) sleep and muscles are always flaccid, in contrast to seizure disorders where increased muscle tone is often present. Syncope can have features of seizures or can be the cause of seizures. Electrocardiogram (ECG) and, eventually, Holter monitoring should be considered in older cats presented with collapsing episodes, and that have no structural brain disease. Correctly differentiating complex partial seizures from syncope in cats with highgrade atrioventricular block can present a real challenge.

Next, the owner should be questioned about the presence of abnormality in between the seizures.

Causes of seizures in cats

Seizures refer to a forebrain disorder. Their causes may originate outside (extracranial) or inside (intracranial) the brain ($^{Table \ 1}$).

Extracranial causes of seizures may be found outside the body (toxic disorder) or inside the body (metabolic disorder). Common metabolic causes include hepatic encephalopathy (either due to portosystemic shunt or to cirrhosis), renal encephalopathy, ionic imbalance (hypocalcaemia, hyponatraemia, hypomagnesaemia or hyperkalaemia), hypoglycaemia, polycythemia and hyperthyroidism.

Common toxic or nutritional disorders seen in cats include lead, ethylene glycol, organophosphate, carbamate and metaldehyde poisoning, along with thiamine deficiency. Intracranial causes of epileptic seizures can further be divided into functional (primary or idiopathic epilepsy) and structural forebrain disorder (secondary or symptomatic epilepsy). Structural brain diseases include:

- cerebrovascular accident (common known causes in cats include hypertension, intoxication by anticoagulant and parasitism);
- infectious encephalitis (feline infectious peritonitis [FIP], feline immunodeficiency virus, feline leukaemia virus-associated central nervous system [CNS] lymphoma, toxoplasmosis, Borna disease and bacterial meningoencephalitis);
- immune-mediated encephalitis;
- post-head trauma;
- primary and metastatic brain tumour; and
- anomalous (hydrocephalus).

It is likely that a number of undefined viruses can be the cause of seizures in cats without necessarily causing inflammatory changes within the brain.

Some cats may present with an unusual pattern of seizure activity, with sudden severe cluster seizures associated (or not) with neurological signs. Diagnostic test results (metabolic profile, magnetic resonance imaging [MRI] scan of the brain, cerebrospinal fluid [CSF] analysis and infectious titres) are usually normal or may reveal very mild CSF changes. The latter may reflect severe seizure activity or mild inflammatory/ infectious process. The prognosis for cats with

suspected viral encephalitis is generally good, with only supportive therapy and a short course of antiepileptic treatment. Primary (or idiopathic) epilepsy is considered less common in cats, compared to dogs.

Why do a neurological examination?

A thorough neurological examination is essential to detect abnormalities other than the seizures.

The neurological examination should primarily focus on evaluating for forebrain dysfunction by assessing mental status and behaviour, abnormal posture (such as head turn), gait pattern (such as propulsive circling), postural reactions, menace response and response to nasal stimulation. The examination may reveal:

- no abnormalities;
- diffuse/symmetrical forebrain abnormalities;
- focal/asymmetrical forebrain abnormalities; or
- multifocal CNS abnormalities.

A completely normal neurological examination is compatible with idiopathic epilepsy.

Cats with intracranial disease may also have a normal neurological examination if the causative lesion is located in the "clinically silent" areas of the forebrain, such as the olfactory bulbs. Occasionally, metabolic disease may wax and wane, resulting in a normal neurological examination. However, the presence of concurrent systemic signs may indicate the presence of an underlying metabolic disease.

Diffuse symmetrical forebrain abnormalities should prompt consideration of an extracranial cause (metabolic or toxic). If the cat is examined shortly after a seizure, these types of symmetrical signs may represent postictal signs. The determination of unilateral brain dysfunction in the interictal period often suggests a structural intracranial cause of the seizures.

Multifocal CNS abnormalities are also suggestive of structural intracranial causes, but narrow the differentials to inflammation, infection, multiple primary brain tumour (such as multiple meningioma) and metastatic neoplasia (such as lymphoma).

Diagnostic approach

Baseline blood work – including a complete blood count, chemistry profile, bile acids, blood pressure, as well as a urinalysis – should be performed in all cats with seizures.

These non-invasive tests may help to rule out metabolic causes of seizures and are useful in planning anaesthesia for any advanced imaging. Investigation of intracranial causes involves the use of advanced imaging modalities of the brain (MRI or computed tomography) and CSF analysis.

A CSF tap is indicated if the imaging is normal or is suggestive of intracranial disease and the cat is believed to have normal intracranial pressure. If there is a large space-occupying mass, or there is evidence of brain herniation, a CSF tap is contraindicated.

Cultures and infectious disease titres (FIP, toxoplasmosis and cryptococcosis) may also be useful tests to perform on CSF. The diagnosis of primary epilepsy is unfortunately a diagnosis of exclusion after eliminating extracranial causes and structural forebrain disorder. To date, no definitive test exists to confirm this diagnosis. A seizure focus incompatible with an idiopathic origin, but not readily identifiable as a structural defect on MRI and CSF analysis, is referred to as cryptogenic.

Management

Unless idiopathic or cryptogenic epilepsy is considered to be the primary differential for the seizure activity, specific treatment of the underlying cause is essential and the success of this will determine the need for symptomatic seizure therapy.

The aim of any antiepileptic treatment is to "control" the seizures by reducing their frequency, intensity and severity with minimum side effects. The decision to start antiepileptic treatment is still controversial. Cats with a single seizure or isolated seizures separated by long periods of time do not require treatment. Treatment is indicated when:

- the first seizure is lifethreatening (status epilepticus or severe clusters);
- multiple seizures are observed in a short period;
- seizures occur more than once a month and/or owners object to their frequency;
- the seizures are becoming more frequent or more severe; or
- an underlying progressive intracranial disorder has been identified as the cause of the seizures.

Commonly used antiepileptics in cats are summarised in Table 2. The author does not recommend the use of oral bromide in cats due to the high incidence of side effects (clinical and radiographic signs similar to feline asthma).

Phenobarbital is the first choice of many clinicians for cats with seizures. In dogs, repeated phenobarbital administrations are known to alter estimated steady-state serum concentration as a

consequence of enzyme induction. This results in the need to progressively increase oral dosage with time to maintain steady-state therapeutic level. This phenomenon of enzyme induction following repeat administration of phenobarbital is negligible in cats. The elimination half-life is stable at around 34 to 43 hours and, therefore, drug concentrations of phenobarbital are not expected to decrease in cats receiving long-term therapy without changing the oral dosage.

Monitoring of serum level is only justified shortly after the onset of treatment (when steady-state level is reached after eight to 12 days) due to the differences in elimination kinetics of phenobarbital between populations of cats or when drugs that might interfere with phenobarbital's pharmacokinetic are added.

Recommended therapeutic ranges have not been properly defined in cats, but are considered similar to the recommended one in dogs (20mg/dl to 35mg/dl).

Cats should not be considered as refractory to treatment until serum phenobarbital concentrations reach 35mg/dl unless unacceptable side effects persist. In case of poor seizure control, a second antiepileptic drug should be considered if serum phenobarbital levels are well within the therapeutic range and/or the cat does not tolerate higher doses of phenobarbital.

Oral levetiracetam or pregabalin is the author's choice for additional antiepileptic drug (Table 2). These drugs can also be used instead of phenobarbital in case the cat develops severe side effects, such as cutaneous eruption or generalised lymphadenopathy (delayed hypersensitivity to phenobarbital).

None of the drugs mentioned in this article are licensed for use in cats.