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WORK-UP, THERAPY AND COMPLICATIONS OF SEIZURES IN DOGS
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INTRODUCTION
It is important to define the terminology used in the context of this presentation as it greatly affects this speaker’s diagnostic and therapeutic approach to recurrent seizures in dogs. In the context herein, the epilepsy is idiopathic when there “is only epilepsy, with no underlying structural brain lesion or other neurological signs or symptoms; idiopathic epilepsy is presumed genetic and usually age dependent”.1,2 This definition implies that the patient has had a thorough diagnostic work up that includes magnetic resonance imaging (MRI) of the brain and cerebrospinal fluid (CSF) analysis. The epilepsy is symptomatic when “the epileptic seizures are the result of one or more identifiable structural lesions of the brain”.1,2 The epilepsy is probably symptomatic when “the epilepsy is believed to likely be symptomatic but no etiology has been identified”.1,2 The following presentation is the summation of over 25 years of medical neurology referral practice. The objective is to increase the knowledge of the practicing veterinarian as it relates to seizure activity in the hope to improve seizure control and ultimately increase the lifespan of epileptic dogs.

SEIZURE PATTERN AND DIFFERENTIAL DIAGNOSIS
An epileptic seizure is a diagnostic entity with etiologic, therapeutic and prognostic implications.1,2 The cause of seizure in a given patient is intimately linked to the seizure pattern. The seizure pattern includes the breed of the animal, its age at onset of seizures, the seizure type (focal, focal onset with generalization, or generalized) and, the frequency of seizures. A Doberman with seizures, regardless of the age, is suspicious for symptomatic epilepsy because seizures are so unusual in this breed. The same is not true for the Labrador retriever or the German shepherd dog. However, when one of these dogs is presented at 7 years of age with a first seizure, a diagnosis of idiopathic epilepsy cannot be given without serious consideration to structural causes of seizures. Idiopathic epilepsy should never be diagnosed in a dog older than 5 years, or younger than 6 months without a thorough diagnostic work up. Genetic/idiopathic epilepsy has been reported in Finnish Spitz dogs in which all seizures were focal seizures.3 This may occur with idiopathic epilepsy but is far from being the rule. In most cases, the seizures have a focal onset with rapid secondary generalization or, remain focal.4,5,6 First onset seizure presented as a cluster of seizures or status epilepticus, is usually not observed with idiopathic epilepsy. Symptomatic epilepsy is more commonly observed with clusters of focal seizures that progress over a few days to generalized seizures and/or status epilepticus. In dogs showing status epilepticus as the first manifestation of a seizure disorder, intoxication should always be considered.7

At our institution, the most frequent causes of seizures are, by order of frequency, ‘probably symptomatic epilepsies’, encephalitides and cerebral tumors. The most frequent tumor is the meningioma of the large breed dog.

DIAGNOSTIC WORK UP
For many veterinarians, most dogs presented with recurrence of seizures end up with a diagnosis of idiopathic epilepsy if the blood work and the physical and neurological examinations are normal. A thorough diagnostic work up with MRI of the brain and CSF analysis is frequently perceived as not necessary by the veterinarian. This is unfortunately also the case for many of the retrospective studies published on the subject of idiopathic epilepsy despite the fact that focal seizures and seizures with a focal onset are the most common seizures in dogs. In all instances of focal seizures (with or without generalization), the seizure originates from a focus of abnormal cerebral parenchyma. Moreover, of the neurological tests targeting the cerebral hemispheres, the mental status is the most difficult to evaluate because it necessitates the owner’s ability to recognize mild to moderate but consistent behavioral changes in their animal. This is particularly true with the epileptic dog. Clinical experience has shown that owners of dogs, with significant MRI cerebral lesions involving the frontal and temporal lobes, are poor at evaluating their pet’s behavior. Regardless of the dog’s age, it is wise to assume that the presence of focal seizures or seizures with focal onset harbors a focal cerebral lesion. Low field MRI is not ideal in the diagnosis of canine epilepsy, especially when the dog is described as mentally normal by the owner. Magnet strength is important as low field MRI may not succeed at demonstrating smaller lesions. It has been demonstrated that age at onset of seizures is not a good predictor of MRI results.8 Ideally, a diagnostic work up that includes physical, neurological and ophthalmological examinations, CBC, biochemical profile and urology, MRI of the brain and CSF analysis should be performed in any dog presented with recurrence of focal seizure or seizure with focal onset. If the preliminary results are suggestive of metabolic or neoplastic disease, thoracic radiographs (3 views) and abdominal ultrasound are added prior to anesthesia for neuroimaging. In inflammatory diseases, titers or PCR of infectious diseases encountered in the area are pursued as well. In most ‘probably symptomatic epileptic’ dogs, an endocrine panel including thyroid profile (T4 and TSH) and baseline cortisol is also requested.

When the criteria for the diagnosis of idiopathic epilepsy are applied stringently, one realizes that the syndrome is not as frequent as previously reported. Most dogs with recurrent seizures are affected with symptomatic or probably symptomatic epilepsy. There is benefit for the patient in categorizing its epilepsy as “probably symptomatic” when the seizure pattern detracts from idiopathic epilepsy because it forces the clinician to diagnostically reevaluate the patient every time he is presented to the office.

THERAPEUTIC PLAN
Treatment failure in a great majority of cases, results when the wrong diagnosis is posed, the wrong treatment given, the wrong antiepileptic drug (AED) chosen or, when the AED is used inadequately. The seizure pattern has a determining role not only in the establishment of the differential diagnosis but also in the therapeutic plan. In symptomatic epilepsy, the successful control of seizures is intimately associated to the successful treatment of the primary cause of seizures. As an example, the
cerebral menigioma of a dog with seizures must be addressed to improve seizure control. In cases where surgery is not an option, an anti-inflammatory treatment such as low dose dexamethasone will be more successful at improving seizure frequency than antiepileptic treatment alone.

In all patients with idiopathic or probably symptomatic epilepsy, the primary treatment is the antiepileptic treatment. The choice of an antiepileptic drug (AED) is based on the type of seizures present, the general health and age of the animal, the family lifestyle and the cost of the drug. Focal seizures or seizures with focal onset are more likely to respond to treatment when the AED targets this type of seizures. It is also important to use the AED adequately measuring serum levels whenever available. By order of frequency, the AEDs used in the maintenance treatment of canine epilepsy include phenobarbital, potassium bromide, zonisamide (5mg/kg q12h when it is used as sole agent and 10/kg q12h if the dog receives simultaneously phenobarbital)9, 10, levetiracetam (10mg/kg q8h)11, gabapentin (10mg/kg q8h)12 and clonazepam or clorazepate.

Veterinarians have somewhat neglected the quality of life of the epileptic patient. For years, the only antiepileptic drugs (AEDs) available and used to treat canine epilepsy were phenobarbital (1912) and potassium bromide (1857). Despite the side effects of these drugs, in a recent survey, 82% of the respondents used a combination of phenobarbital and potassium bromide to manage refractory seizure disorders in dogs.13 However, today, there are other options and owners are willing to pay extra cost to avoid the side effects of the older agents. Although phenobarbital remains one of the most potent and most used AED in the treatment of canine epilepsy, as experience is gained with the newer AEDs, its use will gradually diminished. In this author opinion, potassium bromide should be restricted to dogs with intractable generalized epilepsy when everything else has failed. Its long half-life, the polyuria and polydipsia, and the polyphagia with weight gain that ensue render its use problematic. Levetiracetam is reported as mainly efficacious against focal seizures but its use for focal seizures with secondary generalization is increasing, and, in selected cases, has been successful. The only side effect reported is an occasional mild sedation at onset of treatment. To avoid the sedation often present with AEDs at onset of treatment, it is advised to initiate treatment gradually, treating once per day or giving half of the dose for a few days, if the seizure frequency allows it. Zonisamide has proven effective for generalized and focal seizures with occasional mild sedation. Gabapentin in the author’s experience has not been as effective in the treatment of refractory epilepsy as compared to the AEDs mentioned above. It is safe, has no know drug interaction and only mild to moderate sedation at onset of treatment. The benzodiazepines have been supplanted with newer more efficacious AEDs for maintenance therapy. Epileptic dogs frequently become refractory to this group of AEDs.

COMPLICATIONS OF SEIZURES

The most common deleterious complication in epilepsy is the development of status epilepticus (SE). A substantial percentage of idiopathic epilepsy (IE) dogs have episodes of SE.14 Dogs with greater body weights are more likely to have episodes of SE. Early appropriate seizure treatment does not appear to decrease the risk for dogs to have episodes of SE.14 Premature death is also reported in dogs with epilepsy15 with survival time being shorter for dogs that experience episodes of SE.14

The most frequent complications encountered in epileptic dogs relate to the antiepileptic treatment. The phenobarbital-induced hepatotoxicity, once quite common, is now rarely observed. Veterinarians and owners are well aware of the necessity to follow the AED levels and liver biochemical profile.16 The use of phenobarbital and/or KBr increases the probability of pancreatitis.

The most deleterious and insidious effect of the use of phenobarbital and/or potassium bromide is the tremendous weight gain that occurs in the first few months of treatment in most dogs. The weight gain has detrimental effect on the joints with secondary cruciate rupture, ataxia, somnolence, lethargy, and fatigue.

CONCLUSION

When the criteria are used stringently, IE is not as common as previously observed at least in this author’s opinion. It is important to encourage the diagnostic work up of dogs with focal seizures or seizures with focal onset. Many of the newer AEDs are efficacious in the treatment of canine epilepsy without the deleterious effects associated with the use of the older agents, phenobarbital and KBr.