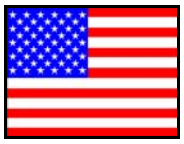

Seizures in Dogs - Part 2

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See Issue 3 of 2011 (pages 120-121) for Part 1

Fig 1 **Seizure Pathophysiology**

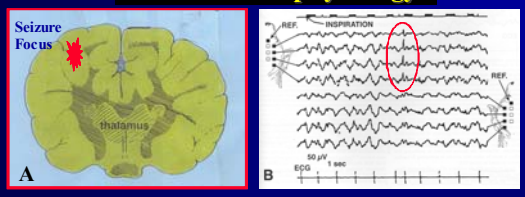

Fig A. The seizure focus (red spot) is the area of the brain where the abnormal electrical activity or paroxysmal discharge (PDS) originates.

Fig B. This abnormal electrical activity may be recordable on an EEG (spikes outlined by the oval red) even when the patient is not having seizures. In order to have the clinical manifestation of seizure, the neurons at the seizure focus they have to reach a critical number and they must to become synchronized into the paroxysmal firing.

Diagnosis

1. **General History:**

Signalment, presenting signs, Immunization history, medical and surgical history, Environment, Indoor/outdoor, Toxin exposure, Travel history, Body system (e.g., vomiting, diarrhea, urination/defecation, coughing), nutritional status.

2. **History Specific to seizures:**

A detailed and accurate history is the cornerstone of diagnosis. The owner should be asked age of seizure onset, seizure frequency and description of the seizure. Any focal signs at the start of the seizure such as turning the head to one side or jerking to one limb may be useful for the seizure focus localization in a specific area of the brain and to classify the seizures. The owner should be asked if the event occur at a certain time of the day, or in association with other situations such as exercise, noise, stress etc. The owner should be also asked if there is any known or suspected familial history of seizures, birth complications, previous encephalitis, or previous head trauma. Client should be asked whether or not any interictal abnormalities, such as change in behavior, gait, appetite, weight, or sleep habit have been observed. Finally, owner should be asked if the dog is treated with anticonvulsant drugs, and response to therapy. Careful questioning of the owner is required to determine whether the episode described was actually a seizure. Owner may often confuse syncope or acute vestibular syndromes with seizures. A video of the patient seizure event is of a great value.

3. **Physical and Neurologic examination:**

a. A complete physical examination may detect signs or systemic illness that may be suggestive of an underlying cause for the seizures.
b. The neurologic examination may detect persistent neurologically deficits. Intracranial focal lesions often cause detectable deficits in the postural reactions such as delay in proprioception on one side and monolateral blindness. However, it is important to remember that abnormalities detected just after the seizure event may be just temporary postictal deficits and not necessarily associated with a persistent brain lesion. Repeating the examination at a later time may be indicated in this case.

4. **Minimum data base:**

a. Complete Blood Count, Serum biochemical profile (fasting), Urinalysis (to rule out metabolic disorders)
b. Thoracic radiographs (to rule out infectious or metastatic disease)
c. Abdominal ultrasound (to rule out portosystemic shunt or metastatic diseases)

5. **Extended data base:**

a. Serum bile ac. determination (pre and post prandial); particularly in young dog to identify porto-systemic shunt
b. Thyroid function; in adult dogs, because of the possible link between hypothyroidism and seizures.
c. Serum lead level determination; in patients with possible exposure to lead.

6. **Ancillary Diagnostic testing:**

a. Magnetic resonance imaging (MRI) and cerebrospinal fluid analysis (CSF). These tests are indicated in dogs with interictal neurologic deficits, focal seizures, seizures refractory to drug therapy, or an onset of seizures in young animals (less than 1 year old) or in dogs older than 5 years.
   i. MRI is able to detect brain tumor, encephalitis, vascular event (stroke, bleeding), congenital or developmental abnormalities (e.g., hydrocephalus, cyst).
   ii. CSF includes cell count, total protein concentration, +/- bacteriological study. CSF is performed when the MRI is suggestive of encephalitis or when the MRI is normal.
b. Electroencephalography is not commonly performed. This test is usually performed in research center. Electroencephalography records electrical activity only from the superficial cerebral cortex; if the seizure focus is deepest in the cerebral cortex it will not be detected. In addition, artifacts from the electrical muscle activity of the thick temporalis muscle preclude a deeper cerebral cortex recording.

THERAPY

General principles of anti-seizures therapy.

The overall goal of anti-seizure therapy is to have a seizure free patient; however, this goal is rarely achieved. In the majority of the dogs, the seizure frequency may be decreased and the seizure intensity may be alleviated to the point that the patients may have a normal life (without intolerable or life-threatening adverse effects from the medication) and the owner doesn't fill too much distress.

1. **When it is recommended to start the medication?**

a. More than 1 seizure in 2 months
b. Cluster seizures (2 or more seizure in 24 hours)
c. Episodes of status epilepticus
d. In dogs with symptomatic epilepsy. In these patients, therapy should be started immediately while addressing the underlying cause. As example in patient with benign and surgically accessible brain tumor such as meningioma, the surgical resection should be considered; in dogs with encephalitis appropriate specific therapy should be given, in dogs with hypertensive hydrocephalus the appropriate shunting of the outflow obstruction should be provided; etc. These specific treatments will be in place or in addition to the anti-seizure therapy.

seizures or the initial presentation is status epilepticus, aggressive antiseizure therapy is indicated. Some animals have marked aggression in the pre- or post-ictal phase, which can be intolerable to the clients and their families.

f. In dogs with Idiopathic epilepsy. In these patients antiseizure therapy is usually started after waiting for the second seizure episode. This gives a baseline of the seizure frequency and help to assess the efficacy of the therapy. In dog with less than 3 seizures per year, and with mild seizures, anti-seizure therapy may not be needed; it will be given only if there is a trend for the seizures to become more frequent.

g. In dogs with idiopathic or cryptogenic epilepsy anti-seizure therapy is usually given for the rest of the patient live. However, if the patient is seizure free for 6-12 months, a careful and slowly reduction of the antiseizure drugs dose may be attempted.

2. **Selection of the appropriate anti-seizure drug**

The efficacy of an anti-seizure drug depends on its blood concentration, and on its ability to remain in the patients long enough at the therapeutic concentration. The absorption and the elimination of the various anti-seizure drugs differ considerably between different species. Only a few of the anti-seizure drugs are suitable for use in dogs, while the vast majority used in people are not either well absorbed or are rapidly eliminated from the blood. As a general rule, treatment with a single drug should be attempted initially. Phenobarbital and Potassium bromide are the most commonly used anti-seizure drugs in dogs. However, in the last few years with the introduction of other effective anti-seizure drugs in dogs, potassium bromide is becoming less popular. Refractory Epilepsy: Although seizure frequency and severity may be reduced in the majority of dogs treated with anti-seizure drugs, 25% of the dogs may have refractory epilepsy. Epilepsy is refractory when the patient's quality of life is compromised by frequent or severe seizures despite appropriate drug therapy.

3. First-Line Anti-seizure drugs.

A. Phenobarbital

neuronal cell membrane (called GABA receptors), increasing the duration of opening the channel and facilitating the intracellular inflow of Cl-. The increase negative charge inside the neurons is called hyperpolarization, which make the neuron less prone to create an electrical discharge and consequently a paroxysmal electrical discharge.

b. It is metabolized primarily by the liver.

c. Ten to 15 days are required to reach a steady concentration in the blood. This way serum level should be checked 2-3 weeks after initiating therapy or changing the dose.

d. The initial dose is 2.5-3 mg/kg orally every 12 hours. The therapeutic range is 15-40 ug/ml .

e. Cost: inexpensive.

f. Adverse effects:

i. Sedation, ataxia, increase in eating, drinking and urinating are common dose dependent side effects. Sedation and ataxia often improve after several weeks of therapy.

ii. Occasional over-excitement.

iii. Blood abnormalities (blood dyscrasia): including anemia (low red blood cells), neutropenia (low white blood cells), and thrombocytopenia (low platelets), have been reported. It is important to recognize these abnormalities by checking the CBC (complete blood count) at 3 and 6 months after starting the therapy. If not detected on time, these blood abnormalities may become life-threatening situations. This is an idiosyncratic reaction and discontinuation of the Phenobarbital will resolve the problem.

iv. Liver toxicity: rare, this risk increases with blood concentration higher than 35 ug/ml. Elevation of liver enzymes (ALP, ALT, GGT, AST) is common. This does not necessarily indicate clinically significant liver disease or the need to stop therapy. Bile acids are a better test to assess liver toxicity and are checked every 6-12 months to screen for liver disease, which is usually reversible if detected early and the drug stopped.

v. May decrease blood Thyroid hormone level, without inducing clinical signs of hypothyroidism.

TO BE CONTINUED ISSUE 1 OF 2012