Diagnosing Seizure-like Episodes: Startling Results of EEG Video Case Studies

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Introduction

The International League Against Epilepsy (ILAE) defines seizure as the transient occurrence of signs, symptoms or both due to abnormal excessive or synchronous neuronal activity in brain. Although this seems straight forward, there are many events that cause a transient occurrence of signs, symptoms or both that are NOT from abnormal excessive or synchronous neuronal activity in the brain. These events are seizure-like and masquerade as a true epileptic seizure. Without assessment with Electroencephalography (EEG) these events could be falsely classified as seizure. Conversely, abnormal excessive or synchronous neuronal activity in the brain does not always have a detectable transient occurrence of signs, symptoms or both. Therefore using observation alone, without EEG, would lead to events being falsely classified as not seizure. The goal of this talk is to provide video and EEG from cases that are seizure-like such in order to improve your ability to detect true epileptic seizure.

Role of EEG

In human medicine EEG is used to discriminate movement disorder, psychogenic events, metabolic disease from true epileptic seizure. EEG is also used to detect subtle or non-convulsive seizure and then evaluate the effectiveness of anti-epileptic drug (AED) therapy. We have EEG in all 4 of our clinics as well as an intramural EEG certification program for our technical staff. The EEG is read with the assistance of an extra-mural physician expert in the interpretation of both human and animal EEG. We perform EEG for the exact same reason it is performed in human medicine.

Intracranial and Extracranial Activity During Seizure

An imbalance between excitatory and inhibitory neurotransmitter activity autonomous neuronal depolarization. With recruitment a group of neurons synchronize and depolarizes / repolarizes autonomously and spreads within that hemisphere of the brain due to failure of spatial containment. This hypersynchronous electrical activity then crosses to the other hemisphere capturing the entire brain before eventually being contained, usually within 2 minutes. During the seizure there is excess glutamate release, calcium influx, opening of sodium channels that can lead to temporary neuronal dysfunction or with prolonged seizure, neuronal death.

In the **pre-ictal state**, as the focus is developing and spreading the patient may experience abnormal visual, auditory, physical, or autonomic nervous system abnormalities manifested as staring off into space, searching a room, restlessness, clingy behavior, fly biting, circling, odd vocalization, a limb becoming stiff or rhythmically moving, elevated heart rate, dilated pupils, salivation, vomiting.

In the **ictus or seizure**, the focus has captured both cerebral hemispheres and the patient may experience loss of consciousness, collapses, rigidly extend the neck and all 4 limbs. The hypersynchronous or rhythmic nature of the electrical focus can be noted as paddling or all 4 limbs. A failure to control and regulate the breathing can manifest as apnea and paradoxical breathing where the diaphragm and intercostal muscles are not working together. Perturbations in the autonomic nervous system can lead to bradycardia or tachycardia, profuse salivation, urination, defecation, miosis or mydriasis, and piloerection. The **post-ictal period** results from excitotoxicity and typically lasts 30-30 minutes where the patient emerges from being confused, blind, weak, and side-stepping. If the seizure is not recognized (non-convulsive) or difficult to treat neuronal necrosis and death can result from seizure.

Practical Criteria for Distinguishing Seizure

In a recent paper the inclusion criteria for seizure was when 3 of the 4 of the following were noted.

1) Salivation, urination or defecation
2) Tonic or tonic-clonic posture or movements or rhythmic contractions of facial or appendicular muscles
3) Decreased responsiveness intra-ictally
4) Postictal phase in which abnormal behavior or mental state was noted

Generally episodes that do not have 3 of the 4 criteria are classified as seizure-like and may or may not be manifestation of abnormal electrical activity or true epileptic seizure. There are many episodic expressions of disease or events that are seizure-like but not seizure (Table 1). Therefore using

observation alone to detect seizure in these cases would cause a false positive assertion that these event were seizure, delayed diagnosis and treatment of the underlying cause and the needless and potentially harmful application of AED.

Electrical Seizure and Electrical Status Epilepticus

An electrical seizure is defined as ictal discharges consisting of a rhythmic pattern with definitive evolution in frequency, amplitude and/or morphology persisting for at least 10 seconds. Electrical seizure can occasionally manifest as convulsions (generalized tonic-clonic) with patient flailing on its side, paddling all 4 limbs or holding the limbs, head and neck in rigid extension. A non-convulsive seizure (NCS) is defined as a seizure where there is no overt convulsive movements. Another term used for non-convulsive seizure is complex partial seizure where there is only an acute alteration in consciousness. NCS is more common than convulsive seizure in people and cats, and potentially dogs as well. When an electrical seizure lasts for more than 30 minutes it is almost always non-convulsive and termed electrical status epilepticus or non-convulsive status epilepticus (NCSE).

Seizure Frequency and Status Epilepticus

Terms to describe seizure frequency from best to worst prognosis include: sporadic seizure, cluster seizure, acute repetitive seizure, convulsive status epilepticus (CSE), non-convulsive status epilepticus (NCSE), refractory status epilepticus (RSE), super-refractory status epilepticus, or malignant status epilepticus. A cluster seizure is 2 or more seizure within 24 hours and acute repetitive seizure is 2 or more seizure within 5-12 hours. When seizures are prolonged and without a return to baseline, they are referred to as status epilepticus (SE) with the best studied form being CSE. The original definition of SE was a 30 minute or longer continuous seizure because animal models show neuronal damage and seizure become self-sustaining after 30 minutes. However the current definition of a SE is a seizure lasting 5 minutes or longer, 2 seizures where the patient is unable to respond to commands or walk between seizures, or when patient is still seizing. This definition has evolved because clinicians no longer want to delay a patient's entry into a protocol for SE since prompt therapy is required for a good outcome. In human medicine, about 150,000 people are thought to develop CSE per year in the USA. In dogs with idiopathic epilepsy (genetic or unknown cause) the rate of cluster seizure is reported at 41-94% and for CSE 53-69%. These conditions are common and important problems in both veterinary and human medicine.

Progression from Convulsive to Non-Convulsive Status Epilepticus

During CSE treatment with benzodiazepines (BDZ) can be ineffective due to endocytosis and changes to the GABA receptor. In this same period of time the convulsions often stop and the electrical seizure can persist despite no obvious convulsions, which is called non-convulsive status epilepticus (NCSE) (Foreman). Refractory status epilepticus (RSE) is diagnosed when electrical seizure activity persists despite treatment with 2 anti-epileptic drugs (AEDs) at appropriate doses – refractory SE is typically non-convulsive. When RSE persists for greater than 24 hours it is super-refractory SE and when SE returns within 5 days of tapering anesthetic medications used to treat SE, then it is called malignant SE.

NCSE Diagnosis Requires EEG

As the video cases will demonstrate many of our patients with NCSE appeared to be asleep or comatose. This is common too in people. A paper concludes that many people with NCSE appeared to be sleeping and that "clinical detection of NCSE would not have been possible with routine neurologic evaluations without use of EEG monitoring". The signs of NCSE can range from mild confusion or disorientation to coma. NCSE should be suspected following a convulsive seizure when there is no improvement in 20 minutes or failure to return to baseline in 60 minutes. Distinguishing NCSE from conditions that mimic seizure can be difficult and about 25% of human patients can have subtle movements that are not from seizure. In human medicine studies have demonstrated some positive symptoms indicative of NCS/NCSE and negative symptoms indicating clinical signs are not from seizure. No such published criteria exist in veterinary medicine. However, in our population of patients with NCSE we noted subtle twitching of ears

or facial muscles, confusion, transient hyperthermia, episodic and unexplained changes in respiratory rates, mydriasis, or coma.

Retrospective Study at Bush Veterinary Neurology Service

In a recent retrospective of 89 dogs and 15 cats where EEG was performed to evaluate seizure-like events there were many cases of metabolic disease, movement disorders and psychogenic events that appeared as seizure. Many of these cases will be presented during the talk. In this study, 21/104 (20%) had electrographic seizure and 21/104(12%) had electrographic status epilepticus. Non-convulsive seizure was noted in 13/15 (87%) of these cases and manifested as coma, twitching of the ears or facial muscles, pupil dilation, paroxysmal elevations of temperature or respiratory rate. The incidence of electrical seizure, non-convulsive seizure and non-convulsive status epilepticus in this study mirrored findings in pediatric and adult studies of hospitalized human patients.

Significant differences in mortality was noted in this study. 50% for patients with electrical status, 47% with electrical seizure and 19% when there were no electrical seizures. A higher mortality and disability rate has also been found in humans and independent of the patient's age or underlying diagnosis. This suggests that electrical seizure detection and treatment can reduce mortality in veterinary patients.

Predictors of Electrical Seizure / Electrical Status

Because EEG is rarely available to the veterinary practitioner we examined factors that might predict a patient is experiencing electrical seizure or electrical status. Observations that help in predicting an event is correlated with electrical seizure include younger age, less time since last seizure and having a history of cluster seizure. A striking finding in the for electrical status was that patients with a history of having had luster seizure were 9 times more likely to have electrical status. The take away message was two-fold, seizure-like episodes are hard to define with out EEG and cluster seizure prevention may help to prevent the deadliest form of seizure (electrical seizure or non-convulsive seizure).

Treating Suspect Electrical Seizure

In recent human study of 164 patients presenting for convulsive status epilepticus (defined as a seizure lasting more than 5 minutes, 2 seizure without becoming normal between or seizing at presentation) patients were treated with a standard protocol for status epilepticus. Once the convulsive seizure resolved, patients had an EEG and about 50% were found to still have electrical seizure and 14% were in electrical status epilepticus. The mortality rate in the electrical seizure group was 50% and independent of age and underlying diagnosis. This paper also notes that once the EEG was used as the end point for treatment (and not observation), outcomes were thought to improve. In the only current veterinary study of a similar population all 10 of the convulsive status epileptic patients were thought to have electrical seizure. Whether using EEG endpoints to determine how much seizure medication to give is the best method of treating electrical seizure remains unknown. More importantly, what if you do not have an EEG available for this purpose?

A general recommendation can be to treat a convulsive seizure patient with AED until there are no signs of twitching or autonomic changes. It is advised to give Diazepam 1 mg/kg, IV and Leveteriacetam 60 mg/kg intravenously and then 10 mg/kg boluses of Phenobarbital every 20 minutes provided the systolic blood pressure is greater or equal to 90 mmHG. A total dose of 50 mg/kg can safely be administered to both dogs and cats.

Conclusion

When a patient presents for seizure the veterinarian must ask themselves if the event was a seizure. Falsely identifying events as seizure or failing to recognize non-convulsive seizure will lead to worse outcomes. Although EEG is needed to allow best diagnosis of seizure-like events, a thorough history and examination, considering the list of seizure-like diseases, and being cognizant of varied presentation for non-convulsive seizure can assist in better diagnosis and treatment of seizure-like diseases.

Table 1. Disease Processes with Seizure-like Appearance

▪ Atlantoaxial subluxation
▪ Breed and drug induced dyskinesia / movement disorders
▪ Cataplexy, narcolepsy, rapid eye movement (REM) sleep disorders
▪ Cervical muscle spasm
▪ Chiari-like malformation / syringomyelia
▪ Encephalitis
▪ Exercise induced collapse
▪ Extreme agitation / psychogenic seizure
▪ Feline hyperesthesia syndrome
▪ Head bobbing / Tremor syndromes
▪ Intermittent decerebrate/decerebellate rigidity
▪ Jaw chomping / fly biting / lip smacking from anxiety or GI disease
▪ Metabolic encephalopathy
▪ Myoclonus
▪ Neuromuscular disease
▪ Psychogenic Non-epileptic Spells / Panic Attacks
▪ Syncope
▪ Movement disorder / Gluten sensitivity (Border Terrier)

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