A 10-year-old neutered male 5.0-kg (11.0-lb) domestic shorthair cat was evaluated because of presumed seizures. Two days prior, the cat had a 5- to 10-second episode of nonresponsiveness, left eye twitching, myoclonus, ptyalism, and tight circling to the right; the cat was clinically normal immediately following the episode. One day prior to the initial neurologic evaluation, the cat started having episodes of left facial twitching that progressed to generalized myoclonus, ptyalism, and tight circling to the right; the cat was clinically normal between episodes. These episodes initially lasted 10 to 15 seconds and recurred every 10 to 15 minutes, but they increased in duration and frequency. The cat was admitted to a local emergency clinic for overnight care and treated with intermittent boluses of diazepam (3 boluses of 0.5 mg/kg IV). Despite this treatment, the episodes continued approximately every 10 minutes, but they increased in duration and frequency. The cat was monitored and received fluids, hetastarch, and dopamine IV. Continuous mechanical ventilation was not required. After treatment, the cat developed unclassified cardiomyopathy, azotemia, anemia, and pneumonia. These problems resolved during a 9-month period.

Clinical Relevance—Findings for the cat of this report indicated electroencephalographic evidence of nonconvulsive status epilepticus. Administration of a high total dose of phenobarbital and monitoring of treatment by use of electroencephalography were successful for resolution of the problem, and treatment sequelae resolved. (J Am Vet Med Assoc 2014;244:708–714)
cytometer, 1 nucleated cell/µL (reference range, < 5 nucleated cells/µL; differential cell count, 93% monocytes and 7% lymphocytes). Results of infectious disease testing of the CSF sample for FeLV, FIV, feline coronavirus, Cryptococcus spp, and Toxoplasma spp at a reference laboratory were negative. Because of uncertainty regarding whether the cat’s clinical signs were attributable to ongoing seizure, a probable diagnosis of idiopathic epilepsy of unknown origin (also termed cryptogenic epilepsy) was made.

After testing, the cat received a crystalloid fluid supplementation with 20 mEq of potassium chloride/L (2 mL/kg/h [0.9 mL/lb/h]). Anticonvulsant treatment was continued with phenobarbital (3 mg/kg [1.4 mg/lb], PO, q 12 h), zonisamide (5 mg/kg [2.3 mg/lb], PO, q 12 h), and levetiracetam (20 mg/kg [9.1 mg/lb], IV, q 8 h). Before results of infectious disease testing were available, broad-spectrum antimicrobial treatment with clindamycin (15 mg/kg [6.8 mg/lb], PO, q 12 h) and doxycycline (10 mg/kg [4.5 mg/lb], PO, q 24 h) and anti-inflammatory treatment with prednisolone (0.5 mg/kg, PO, q 12 h) were initiated. The patient responded poorly to treatment during the subsequent 36 hours (clinical signs continued), and findings of neurologic examination remained unchanged. The cat also developed undulating fever (rectal temperature range, 38.2°C [100.8°F] to 40.6°C [105.1°F]). Despite these clinical abnormalities, the cat continued to eat and drink. At this time, the clinical differential diagnoses were encephalopathy (attributable to multifocal brain injury or previously administered medication) or continuing seizures (with subtle clinical signs). Because of the suspicion of seizures and poor response to anticonvulsant treatment, EEG was performed to detect evidence of seizure activity. To facilitate electrode placement, dexmedetomidine (3 µg/kg, IV) was administered. An EEG was recorded initially with 10 subcutaneously placed EEG needle electrodes (length, 12 mm; diameter, 0.32 mm [28 gauge]) positioned at frontal (F1 [left] and F2 [right]), auricular (A1 [left] and A2 [right]), temporal (T3 [left] and T4 [right]), central (C3 [left] and C4 [right]), and occipital (O1 [left] and O2 [right]) locations bilaterally. In the transverse plane, the frontal electrodes were placed 0.5 cm (0.2 inches) rostral to the intersection of the temporal lines (over the frontal sinus), the occipital electrodes were placed at the base of the zygomatic process, and the auricular, temporal, and central electrodes were placed at locations half of the distance along a line from the frontal to the occipital electrodes. In the sagittal plane, the frontal, occipital, and central electrodes were placed at a location one-quarter of the distance along a line from the dorsal midline aspect of the head to the base of the zygomatic process, and the temporal electrodes were placed at a location one-half of the distance along a line from the dorsal midline aspect of the head to the base of the zygomatic process. An additional electrode was placed subcutaneously at the base of the left ear as a ground electrode. The EEG recordings were reviewed in real time by a board-certified veterinary neurologist with experience in evaluation of such recordings (WWB) and a board-certified human electroencephalographer with experience in evaluation of such recordings of domestic animals (MMS). Recording parameters included a time constant of 0.1 second and a high-frequency filter set at 35 Hz; display sensitivity was 3 µV/cm with a sweep speed of 30 mm/s. A 60-Hz notch filter was used to decrease electrical interference. An ECG recording was simultaneously obtained for identification of ECG artifacts and to monitor heart rate. An electro-oculogram was simultaneously recorded with electrodes placed in the periorbital muscles of the left eye for identification of eye movement artifacts; electro-oculogram settings were identical to those used for EEG. All recordings were stored digitally for later review.

Results of evaluation of the initial EEG recording indicated generalized periodic epileptiform discharges that changed in frequency and amplitude over time (Figure 1), alternating with periods of generalized lower-amplitude fast activity with less prominent periodic complexes. This pattern was detected repeatedly with a cycle time of approximately 1 minute. This pattern is commonly detected in EEGs recorded from humans with continuous subclinical seizure activity. Therefore, a definitive diagnosis of nonconvulsive status epilepticus was made for the cat.

After the diagnosis had been determined, a continuous EEG was recorded with 6 electrodes (positioned at locations F1, F2, T1, T2, O1, and O2); an ECG was also recorded (Figure 2). Fewer electrodes were used during this EEG recording than were used during the initial EEG recording because it allowed for easier electrode placement but still provided sufficient information for monitoring of treatment. The EEG recording was continuously monitored by operators (DEC and WWB) during the subsequent 10 hours with intermittent remote live monitoring and interpretation by another operator (MMS). During this time, the cat was treated with phenobarbital (6 mg/kg [2.7 mg/lb], IV, q 30 min) until the ictal EEG pattern ended and a burst-suppression pattern was detected; the total dose of phenobarbital was 108 mg/kg (49.1 mg/lb) administered during a 9-hour period (high-dose phenobarbital treatment period). During this time, the cat became unconscious without any visible motor activity. The cat was intubated to protect its airway; however, there was no loss of voluntary respiration and mechanical ventilation was not required. Heart rate, respiratory rate, rectal temperature, mucous membrane color, capillary refill time, arterial blood oxygen saturation (measured with pulse oximetry), end-tidal carbon dioxide concentration, indirectly measured blood pressure (oscillometric method), hydration status, and urine output were continuously monitored during the treatment period. Hypotension (systolic arterial blood pressure, < 90 mm Hg) was detected in the cat and treated with a bolus of a colloidal solution (5 mL/kg, IV) and subsequent administration of dopamine (3 to 5 µg/kg/min, IV) by means of a constant rate infusion during a 40-minute period; after that time, the cat was normotensive. Warm water bottles were placed around the cat to prevent
hypothermia. Other supportive care during this time included frequent inspection of endotracheal tube placement, periodic manual ventilation to improve gas exchange and lung volume, and placement of a lubricant in the eyes. A blood sample (2.0 mL) was obtained at the end of the high-dose phenobarbital treatment period; serum phenobarbital concentration was 89.0 µg/mL.

Twelve hours after the end of the high-dose phenobarbital treatment period, the patient was still stuporous. A brief follow-up EEG recording was obtained at this time; results indicated a continued burst-suppression pattern and only rare low-amplitude periodic epileptiform discharges. Another follow-up EEG recording was obtained 36 hours after the end of the high-dose phenobarbital treatment period; results indicated the frequency of detection of periodic epileptiform discharges had decreased.

Monitoring and supportive care were continued during the following several days, during which time the cat developed heart failure attributable to an unclassified cardiomyopathy, azotemia, anemia, and pneumonia. No anticonvulsant medications were administered at this time. The cat slowly regained consciousness and was extubated approximately 48 hours after the end of the high-dose phenobarbital treatment period. On day 5 after the end of that period, administration of phenobarbital (2 mg/kg [0.9 mg/lb], IV, q 12 h) was started again. The cat had mild facial twitching on day 6 after the end of the high-dose phenobarbital treatment period, but this resolved after administration of a single

Figure 1—Representative EEG and ECG recordings of a 10-year-old domestic shorthair cat with refractory nonconvulsive status epilepticus. A—Periodic complexes (< 1 per second) are evident. B—Evolution of the frequency of periodic complexes to 2 per second. C—Continued evolution with periodic complexes increasing in frequency to 2 to 3 per second and with a small increase in amplitude. The pattern of periodic epileptiform discharges changes in a consistent manner over time. These EEG recordings were obtained with 10 electrodes interpreted in a 13-channel bipolar montage. The EEG recordings were reviewed in a bipolar modified double banana montage (2 rows of rostral to caudally arranged electrode pairs over each brain hemisphere [1 row laterally and 1 medially]) for the upper 8 tracings and in a transverse pattern for the lower 5 tracings. Initial EEG findings indicated generalized periodic epileptiform discharges that changed in frequency and amplitude over time. The scale for voltage and time is indicated in the figure. A1 = Left auricular electrode. A2 = Right auricular electrode. C3 = Left central electrode. C4 = Right central electrode. F1 = Left frontal electrode. F2 = Right frontal electrode. O1 = Left occipital electrode. O2 = Right occipital electrode. T3 = Left temporal electrode. T4 = Right temporal electrode.
bolus of phenobarbital (6 mg/kg, IV); the maintenance dosage of phenobarbital was increased (4 mg/kg [1.8 mg/lb], IV, q 12 h). On day 9 after the end of the high-dose phenobarbital treatment period, IV administration of phenobarbital was stopped and oral administration of phenobarbital (4.5 mg/kg [2.0 mg/lb], q 12 h) and levetiracetam (50 mg/kg [22.7 mg/lb], q 12 h) was started. The cat was discharged from the hospital 15 days after the end of the high-dose phenobarbital treatment period; oral administration of phenobarbital and levetiracetam was continued. No further clinical signs were detected during approximately 2 months after discharge from the hospital. Results of CBCs and serum biochemical analyses were monitored. Azotemia resolved during the following 3 weeks. Nonregenerative anemia gradually resolved during a 9-month period. Results of an echocardiogram performed 2 months after discharge from the hospital indicated complete resolution of cardiomyopathy.

Discussion

Nonconvulsive status epilepticus represents a state of seizure activity of a duration > 30 minutes in a patient with clinical or behavioral abnormalities without a convulsive clinical manifestation.

Nonconvulsive status epilepticus may include impairment of cognition, subtle facial or limb twitches, head or eye deviation, automatism, or behavioral changes. Because these clinical features may be consistent with diagnoses other than nonconvulsive status epilepticus, confirmation of the diagnosis requires performance of EEG. In humans, nonconvulsive status epilepticus was once
considered rare but is now known to be a common condition (and possibly underdiagnosed), comprising at least one-third of all cases of status epilepticus. This change in the recognized prevalence of the condition is likely attributable to increased accessibility of EEG, particularly in intensive care units.

Nonconvulsive status epilepticus in humans is a heterogeneous disorder with multiple subtypes. Nonconvulsive status epilepticus has typically been classified as focal nonconvulsive status epilepticus (complex partial status epilepticus) or generalized nonconvulsive status epilepticus. Other classification systems have been proposed on the basis of etiology. We used the term nonconvulsive status epilepticus to describe status epilepticus without clinical changes that could be easily recognized as a complex partial seizure; EEG was required to determine that the observed clinical signs were attributable to status epilepticus in the cat of the present report.

Whereas nonconvulsive status epilepticus is increasingly diagnosed in humans, it is likely underdiagnosed in veterinary patients for which performance of EEGs is uncommon in clinical practice. To the authors’ knowledge, this is the first report of EEG-confirmed nonconvulsive status epilepticus in a veterinary patient. Determination of a diagnosis of status epilepticus with EEG is subjective; the interpretation of certain patterns as ongoing electrical seizures or injury patterns is controversial. Therefore, it is important that experienced practitioners be involved in interpretation of EEG recordings.

Convulsive status epilepticus in humans constitutes a medical emergency because it can cause neuro-pathologic damage in the brain (primarily attributable to glutamate-mediated excitotoxicity and the subsequent influx of calcium into neurons). Convulsive status epilepticus can also cause severe systemic disease attributable to comorbidities including hyperthermia, aspiration pneumonia, acute respiratory distress syndrome, and neurogenic edema. Whether the neuronal damage that occurs in patients with convulsive status epilepticus also occurs in patients with nonconvulsive status epilepticus is controversial; the inherent difficulty in differentiating the effects of a causative insult from the effects of a seizure makes research on this topic challenging. Nonconvulsive status epilepticus has been regarded as less dangerous than convulsive status epilepticus because it does not produce the adverse systemic effects of convulsive status epilepticus; however, ongoing seizures may cause brain injury. Prognosis may depend on the underlying etiology rather than the method of treatment of the epileptiform activity. Given that treatment of status epilepticus may cause hypotension and respiratory arrest, some authors have suggested that conservative treatment of nonconvulsive status epilepticus in humans is the preferred treatment method. That opinion has been challenged because of reported adverse consequences related to complex partial status epilepticus, including high mortality rates, cognitive and memory deficits, and MRI changes in the brain. However, outcomes may be more dependent on characteristics of systemic disease than they are on characteristics of status epilepticus. In the absence of overt neuronal damage, nonconvulsive status epilepticus may cause functional changes in neurons that alter electrical excitability of neural circuits.
Results of a study\textsuperscript{31} in which dogs with clinically diagnosed epilepsy were evaluated indicate there is consistency between the clinical diagnosis of a seizure type and the type of EEG abnormalities, indicating EEG is useful for determination of a diagnosis of epilepsy in dogs. Moreover, EEG findings for dogs with epilepsy are markedly similar to findings for humans with that problem. Ketamine has been administered for the management of refractory convulsive status epilepticus in a dog for which EEG findings supported the clinical diagnosis.\textsuperscript{32} Results of another study\textsuperscript{33} indicate EEG is useful for monitoring of dogs and cats with status epilepticus. The EEG findings for the cat of the present report were consistent with those for humans with status epilepticus.\textsuperscript{39} Cats with seizures may have more diverse causes, treatments, and outcomes than dogs with that problem\textsuperscript{40}; therefore, classification of seizures in cats may be more difficult than it is for dogs.\textsuperscript{37} Seizures in cats are typically classified as complex partial seizures.\textsuperscript{3} Hippocampal necrosis has been associated with seizures in cats, but the etiology is unknown.\textsuperscript{6} Results of a recent study\textsuperscript{38} suggest that complex partial seizures with oro-facial involvement are characteristic of this disorder; however, these findings are inconsistent with those of another study\textsuperscript{37} of a larger number of animals. Status epilepticus remains nonconvulsive more often in cats than it does in dogs.\textsuperscript{40} Other authors\textsuperscript{41} estimated that >50% of cats with seizures have nonconvulsive seizures. The authors of that report stated that status epilepticus in cats is difficult to treat and recommended that the aim of treatment should be to stop or substantially decrease the frequency of clinical abnormalities associated with the seizure; they considered phenobarbital to be the treatment of choice. It is our opinion that EEG is clinically useful for evaluation of responses of patients to such treatments.

Despite recommendations for specific placement of EEG electrodes,\textsuperscript{39} there is no standardized recording technique for EEGs in veterinary patients, to the authors’ knowledge. The cause of cardiomyopathy in the cat of the present report was not determined but may have been attributable to the diluent in the drug product\textsuperscript{46,47} or secondary to the seizures.\textsuperscript{48} The cat of the present report had evidence of heart disease for 2 months after administration of a high dose of phenobarbital. After that time, the cat had clinically normal cardiac function.

The present report is the first in which EEG results indicated status epilepticus in a domestic animal. These EEG findings were consistent with those for humans with status epilepticus. This is also the first report in which a cat with status epilepticus was treated by means of administration of a high dosage of phenobarbital.

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