Clinical signs, aetiology and outcome in 30 cats with recurrent seizures (2002-2018)

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ABSTRACT. The purpose of the current study was to describe seizure types, aetiology, treatment response and outcome in 30 cats with recurrent seizures. This retrospective case series study included the medical records of client-owned cats, admitted to the Clinic of Companion Animals for seizure disorders, from 2002 to 2018. Recorded data included history, seizure type, physical and neurological examination findings, blood pressure measurements, complete blood counts, serum biochemistry profile and urinalysis, tentative/final diagnosis, treatment, hospitalization and long-term outcome. A total of 298 feline neurology cases were examined during the study period. Of those, 38 cases were admitted for seizure disorders and 30 met the inclusion criteria. Median age on admission was 38.2 months (3.1 years) (range 2 months- 14 years old). Seizure types, as per owner description, were generalized (26 cats), focal with secondary generalization (3 cats), focal (2 cats) and complex (1 cat). Cluster seizures appeared at least once in 18/30 and status epilepticus in 7/30. Different seizure types were also recorded in individual cases. Fifteen cats (15/30) were hospitalized at least once and the duration of hospitalization ranged from 1-10 days. In most cases, in which diagnosis was established, epilepsy was secondary (25/30), due to previous head trauma (11/30), metabolic (1/30), or inflammatory (4/30) disease, arterial hypertension (3/30), toxicosis (3/30) and intracranial neoplasia (2/30). Congenital hydrocephalus was detected in 1 cat. Tentative diagnosis could not be established in 5 cats; however differential diagnosis included inflammatory or neoplastic encephalopathies. Antiepileptic drug monotherapy (phenobarbital or levetiracetam) was sufficient to control the seizures in 14 cases, while administration of combination therapy with 2 or more antiepileptic drugs was required in 5 cases (phenobarbital, levetiracetam, gabapentin). Successful control was achieved in 11/30 animals for 1-5 years. Seven cats required intensive care at least once due to status epilepticus. Until today, eighteen (18/30) cats are still alive and 11 died or were euthanized. Although in most cases epilepsy was secondary, seizure control was adequate and quality of life (QoL) was improved with antiepileptic drugs when metabolic, inflammatory and neoplastic encephalopathies were excluded.

Keywords: levetiracetam, phenobarbital, post-traumatic seizures, status epilepticus

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INTRODUCTION

Seizures can be primary (idiopathic) or secondary in cats (Bailey and Dewey, 2009). The major categories of secondary disorders in cats include vascular events, encephalitis, neurotoxicoses, head trauma, metabolic disease, neoplasia, congenital and degenerative conditions (Kline, 1998; Bailey and Dewey, 2009). Whether a seizure event is epileptic can only be suspected based on clinical, laboratory, and neuroimaging findings as electroencephalography diagnostic techniques have not yet been developed to contribute diagnostically in veterinary medicine (Pakozdy et al., 2014).

Antiepileptic drugs (AED) administered in cats, include phenobarbital (PB), levetiracetam (LEV), and zonisamide (ZSD) (Bailey and Dewey, 2009; Ukai et al., 2018). The effectiveness of treatment is evaluated by a more than 50% reduction in seizures, thus marking a successful dosage regimen. On the contrary, a reduction of less than 50% or an increase in the number of seizures is indicative of progressive disease, refractory seizures, poor client compliance or inadequate dosing (Bailey and Dewey, 2009).

Comparisons among previous feline epilepsy case series and reviews can be difficult due to different diagnostic methodology and lack of standardized definitions. Follow-up tends to be brief and large case series referring to the full spectrum of seizure disorders in the cat are lacking.

The aim of this retrospective study was to report the seizure types, suspected aetiology, treatment response and long-term outcome in selected feline cases with recurrent seizures.

MATERIALS AND METHODS

In this retrospective study, case records were reviewed from January 2002 to December 2018. From a total of 298 feline neurological cases, 38 cases were admitted for seizure disorders and 30 met the inclusion criteria of the study. These included recurrent episodes of seizure activity, complete records and a minimum of 6-month follow-up period. Epidemiological data and history included breed, age, gender, age of seizure onset, duration of seizure and frequency of seizure activity, previous or concurrent neurological deficits, seizure type (including the presence of cluster seizures or status epilepticus), treatment protocol, antiepileptic drugs with associated side effects and long-term outcome. Physical/ neurological examination, clinicopathological (complete blood counts, serum biochemistry, urinalysis) and diagnostic imaging findings, blood pressure measurements were also recorded. Cerebrospinal fluid analysis, serological tests for Toxoplasma gondii and feline Coronavirus infection were recorded when available. Owners were contacted via telephone when serial re-examinations were not recorded, in order to complete follow-up data (current treatment and status of the cat, frequency of seizures, concurrent neurological or other disorders). Long-term outcome (survival time) started on admission and lasted until the end of the follow-up period for the survived cases and until death for those cats that died. In survived cases, excluding hospitalized animals, follow-up period ranged from 6 months to 12 months.

RESULTS

Feline population of the study

The study population consisted of 23 domestic shorthaired, 5 Persian/Persian crossbred and 2 Siamese cats. Seventeen (17/30) cats were male (11/30 intact, 6/30 castrated) and 13/30 were female (8/30 intact, 5/30 spayed). Median body weight was 4,3 kg for 16/30 cats. Eight cats (8/30) were obese (>4 kg), and 6/30 were <2 kg (kittens and cats with normal body condition).

In 13 cats seizure onset was reported to happen prior to 6 months of age, however the animals were admitted at 1-4 years of age (10/30). Age of seizure onset ranged from 2 weeks to 14 years. All cats were admitted for seizure disorders however the frequency varied among the cats. Fourteen cases were admitted due to the appearance of cluster seizures, eleven cats for increasing seizure frequency ranging from once a month to once a week and four cats for having a first seizure episode.

Seizure activity

Seizures were the only neurological disorder in 23/30 cases. The recorded pre-ictal signs (aura) included behavioral changes. The ictus or actual seizure event was characterized by a variety of abnormal behavioral patterns depending on whether the seizure was focal, generalized or complex. The seizure type included generalized (26 cats), focal with secondary generalization (3 cats), focal (2 cats), and complex (1 cat) seizures. Generalized seizures included tonic-clonic muscle spasms in 20 cats and tonic muscle spasms in 6 cats. Involuntary urination or defecation during seizures was detected in 6 cases. Salivation was apparent in 4 cases, as observed by the owner. Duration of seizure episodes was recorded in 20 animals, and varied from approximately 1 minute (18
cats) to 2-3 minutes (3 cats). Different seizure types were also recorded in individual cases. Complex seizures presented as behavioral changes, rapid running and facial twitching. Aggression developed or continued (post-ictus) after the seizure activity in 8/30 cats. Additional neurological signs were circling in 4 cats, cognitive dysfunction in 3 cats, intention tremors in 1 cat, compulsive behavior (aimless pacing) in 1 cat. Cluster seizures developed at least once in 18/30. Status epilepticus was present in 7/30 cases.

**Seizure etiology**

Due to financial constraints, most of the owners declined advanced diagnostic imaging investigation (CT/MRI). Therefore, tentative diagnosis was based on history, age of seizure onset, clinical course of the disorder (development of clinical signs), clinical and neurological examination, presence or absence of concurrent neurological signs, response to antiepileptic drugs (AED), long-term outcome and necropsy (where available). Diagnosis of metabolic encephalopathy (hepatic encephalopathy) was based on clinicopathological evaluation. Age on seizure onset ranged from 2.5 months to 180 months (median 71.5 months).

Advanced diagnostic imaging was performed in 8/30 cats, one of which was diagnosed with congenital hydrocephalus using ultrasonography, necropsy in 4/30, fundoscopy in 5/30, thyroid profile (T4, fT4, TSH) in 2/30, serological test for *Toxoplasma gondii* or feline Coronavirus infection in 3/30.

Historical evidence and clinical examination presumed the cause of seizures in 17/30 cats. Eleven cats had a history of head trauma, three cats had increased serial blood pressure measurements and there were evidence of toxicity in three cases (application of a canine permethrin ectoparasitic product in 2 cats and organophosphate toxicity in 1 cat).

In most cases, in which diagnosis was established, epilepsy was secondary (25/30), presumed due to previous head trauma (11/30), metabolic (1/30), inflammatory (4/30), toxicosis (3/30), intracranial neoplasia (2/30). Congenital hydrocephalus was detected in 1 cat. In those 4 cats with encephalitis, serological tests for FeLV/FIV infection were negative. From the four cats diagnosed with inflammatory disease, 3 had feline infectious peritonitis (FIP) encephalitis, two died during hospitalization and the other was lost to follow-up. The fourth cat had toxoplasmosis. Tentative diagnosis could be established in 5 cats and the differential diagnosis included secondary encephalopathies. Differential diagnosis in these 5 cats included inflammatory or neoplastic encephalopathies. From these 5 cats, in one cat, primary encephalopathy was suspected.

**Treatment, hospitalization and survival time**

Therapy using one AED was effective in 14 cases (phenobarbital (PB) 9/14, or levetiracetam (LEV) 5/14). Therapy using more than one AED was necessary in 5 cases (4 cats PB+LEV, 1 cat PB+LEV+gabapentin). LEV withdrawal seizures (owner compliance) were observed in 2 cats after a missed dose of LEV. Nineteen cats received life-long antiepileptic medication.

In our study, 14 cats were treated with PB alone (monotherapy, 9/14) or in combination with other AEDs. Of those 9 cats with PB monotherapy, seizure frequency was reduced in 3, while 2 animals had poor seizure response and 4 were lost to follow up. Four cats underwent LEV monotherapy with adequate seizure control while one had poor response. Three cats had good seizure control with PB+LEV combination therapy but one cat was not controlled with the same drug regimen. One cat underwent PB+LEV+Gabapentin therapy but had poor long term seizure control. That cat was previously diagnosed with congenital hydrocephalus.

Fifteen cats required hospitalization (with or without intensive care) at least once (duration range 1-10 days). Seven from those 15 cats required intensive care due to status epilepticus. Five cats died during hospitalization. Euthanasia was elected in 2 cats due to poor control of status epilepticus. Four cats (not the abovementioned) died due to a concurrent disease (3 chronic renal disease, 1 diabetes mellitus). Eighteen cats were alive when the follow-up call was performed and the survival time ranged from 1-12 years. One cat was lost to follow-up.

Successful control (>50% reduction in seizure activity) was achieved in 11 cats with a marked reduction in aggression and improved quality of life (QoL). Eleven cats (11/30) remained controlled for at least 1-5 years. Poor response was noted in 6 cats due to owner non-compliance (3), underlying disease (2), or both (1). Phenobarbital levels were monitored when therapy response was poor in 3 cats.

There were other neurological disorders in both cats with controlled seizures or not. In those cats with poor seizure control, aggression was noted (4 cats). Additional neurological signs included cognitive dysfunction (3 cats), compulsive circling (2 cats), spas-
tic tetraparesis (1 cat), spastic tetraplegia (2 cats), right-sided, absent menace response reflex (1 cat) and bilateral absent menace response reflex (1 cat), ataxia in all 4 limbs (2 cats), blindness (2 cats) and altered behavior (episodes of pointless running, hissing at shadows) (1 cat).

**DISCUSSION**

Secondary epilepsy is reported to be more frequent than primary epilepsy in cats (Pakozdy et al., 2010). This was also observed in the current study, in which a diagnosis of secondary epilepsy was established in 25 cats and was speculated in 5 cats. Presumed post-traumatic epilepsy was the predominant diagnosis in our feline population, while previous studies report intracranial neoplasia as the main cause of seizures (Pakozdy et al., 2010). Data from history were adequate to establish diagnosis as post-traumatic epilepsy because either the owners had witnessed the accident, or the cats were found with external injuries suggesting head trauma.

Antiepileptic drug therapy is recommended when seizures occur post-trauma (Bailey and Dewey, 2009). Eleven cats developed seizures post-traumatically due to head trauma and required antiepileptic medication for controlling them. It has been reported that cats with medical history of mild to moderate head trauma had ≤ 5.6% probability of developing post-traumatic seizures and owners did not observe any seizure activity during the follow-up period (Grohmann et al., 2012). In another study, it was speculated that seizures could appear immediate after head trauma or delayed and thus the owners should be informed about the potential need for antiepileptic drug either at the time of the trauma or in the future; the prognosis was good (Kline, 1998).

Despite the small number of cases diagnosed with FIP encephalitis, the prognosis is known to be poor, as it remains a fatal disease despite the various therapeutic modalities that have been owners (Gunn-Moore and Reed, 2011). In particular, the occurrence of seizures in cats with FIP infection indicates extensive brain damage; therefore it is an unfavourable predictive sign (Timmann et al., 2007). The third case, diagnosed with toxoplasmosis, was still alive 6 months after the first referral. Although the seizures were apparently there, their frequency had been decreased. The prognosis for toxoplasmosis is guarded, due to the potential of recurrence of the neurological disorders (Phoff and Dewey, 2005; Gunn-Moore and Reed, 2011). In our case, prognosis seems to be good in the 6-month-period that we set as follow-up period.

Seizures may result from a wide variety of extra- cranial causes, including toxins, drugs and metabolic disease (O’Brien, 1998). In this study, seizures due to metabolic causes were less frequent (1 case due to hepatic encephalopathy). In previous studies (Barnes et al., 2004; Rusbridge, 2005), hepatic encephalopathy was the predominant diagnosis in the metabolic group of diseases in comparison to others that indicate infrequent seizure occurrence due to hepatic encephalopathy (Kline, 1998). A more recent study indicated a higher percentage of feline seizure cases due to metabolic/toxic causes (Schrieff et al., 2008). Seizures due to toxics appeared in three cats (1 cat was exposed to organophosphates and 2 on permethrin product) in the current study. Thus, in many cats presented with seizures, a careful history of drug use and potential of toxin exposure is essential (O’Brien, 1998).

Vascular diseases include hypertensive encephalopathies and ischemic encephalopathies (Pakozdy et al., 2014). Hypertensive encephalopathies can be the result of chronic renal disease, hyperthyroidism and hypertrophic myocardial pathy (Kline, 1998). In our study, there were 3 cases with hypertension that clinically affected the brain and appeared seizures. All the three cats had a primary disease (2 cats with chronic renal disease and 1 cat with hyperthyroidism), that caused seizures through hypertension.

Two cats were diagnosed with intracranial neoplasia. One of the tumors was histologically confirmed as meningioma but there was no histological examination of the second’s cat tumor. Meningiomas are one of the most commonly observed intracranial neoplasms, appearing with seizures (Tokem et al., 2006).

A tentative diagnosis could only be reached in 5 cases and included secondary epilepsy and differential diagnosis included inflammatory or neoplastic encephalopathy. Final diagnosis was not established because specific diagnostic testing (advanced imaging and cerebrospinal fluid analysis) were not pursued. Thus, these 5 cases whose routine clinicopathological investigation was unremarkable were evaluated for the response to treatment through follow-up. In many cases of feline epilepsy, an underlying cause of seizures was suspected but never proven ante-mortem (Kline, 1998). These include previous post-traumatic, post-inflammatory and post-ischemic lesions that were quiescent and non-progressive (Kline, 1998).
This study indicated that cranial trauma can be a lead

Regarding the type of seizures, cats appear to have generalized seizures more frequently than focal, in the current study. This finding was comparable to those of other studies indicating the generalized sei-

The age of seizure onset range from 2.5 months to 15 years in the present study. The median age of sei-

Phenobarbital (PB) is the current drug of choice in cats with multiple seizure episodes (Berg et al., 2006; Dewey, 2006; Thomas and Dewey, 2008; Finnerty et al., 2014). There are several studies supporting the efficacy of PB of seizure control in epileptic cats (Finnerty et al., 2014); however in our study the number of cats with adequate control of seizures using PB as monotherapy was equal to those cats that are not well controlled. Moreover equal number of cats that underwent PB monotherapy was lost during follow-up period. Probably, whether the number of lost cases was smaller and the study population with PB monotherapy was larger, they could have a different impact on PB efficacy. Adequate seizure control using LEV monotherapy or an adjunctive therapy was superior to those cats that did not. The finding of our study was in parallel with another previous study in which levetiracetam was used as an adjunctive anti-

Although LEV was proved to be superior PB (eit-

In the current study, most cats can improve their quality of life (QoL) and reduce aggression through a successful control (>50% reduction of seizures). The median survival time for seizure cats and the successful control was 1-5 years in our study. Thus, outcome in cats with secondary epilepsy was long in the current study. This finding was in contrast with another previous study in which survival time was shorter in cats with symptomatic epilepsy; however in the same study survival time was longer in cats with probable symptomatic epilepsy (Barnes et al., 2004) indicating that the cause and the degree of the brain damage in secondary epilepsy can influence survival time. Euthanasia was elected in 2 cats, in the current study, due to poor prognosis. This finding is in parallel with another study in which euthanasia was elected soon after a diagnosis was established due to poor prognosis in cats (Barnes et al., 2004) or due to unacceptable seizure frequency in a study with epileptic dogs (Berendt et al., 2007).

Both cats and dogs had a poor prognosis when status epilepticus appear (Bateman and Parent, 1999; Schriefl et al., 2008). Despite the providing data, there was no evidence supporting this hypothesis in our study. More than half of the study population (18/30), appearing cluster seizures, had a good control of seizures. This finding was in parallel with another study performed in epileptic dogs in which the type of seizures was not associated with the survival time (Berendt et al., 2007). Through this finding, it can be assumed that cluster seizures are treatable and not all cats die during hospitalization or soon after that, depending on seizure aetiology. For instance, most cats in our study popu-
lation were post-traumatic cases, with a stable damage in the brain tissue; things could be different if our study population was consisted of cats with neoplastic or inflammatory encephalopathies, which both cause progressive damage to the brain tissue.

Due to the nature of the study, some data were lacking. Advanced imaging tests (CT and MRI) were available in few cases. Cerebrospinal fluid analysis was not performed however it can only diagnose inflammatory encephalopathies and necropsy was performed in few cases. Therefore, the final diagnosis was based mainly on history, follow-up and AED efficacy. Cat population involved in the current study was not a representative population of seizure cats in this area. A possible explanation for this hypothesis is the nature of the clinic, which is a second-opinion clinic and many cases may had been lost before their admission. The sample size was small; therefore it is difficult to draw accurate conclusions. The aim of this study was to offer a general viewpoint on feline cases admitted to a veterinary clinic in the particular geographic location.

**CONCLUSIONS**

The most common cause was post-traumatic epilepsy in this study. The type of seizures did not indicate their aetiology. Cluster seizures appeared frequently and they were not necessarily an indicator of poor prognosis.

Reduced aggression and improved quality of life were noted following antiepileptic drug administration. Survival time in feline seizure patients in this study was apparently longer than time reported on previous studies.

Although final diagnosis was not available, seizure control was adequate and quality of life (QoL) was improved with AED when metabolic, inflammatory and neoplastic encephalopathies were excluded.

**CONFLICT OF INTEREST**

None of the authors had a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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