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Suspected acquired narcolepsy in 8 dogs

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Abstract

Background: Acquired narcolepsy has rarely been reported in veterinary medicine.

Objective: To describe the presentation, clinicopathological features, diagnostic imaging findings, and management of dogs with suspected-acquired narcolepsy.

Animals: Eight dogs with clinical features consistent with acquired narcolepsy.

Methods: A call for suspected cases of acquired narcolepsy was made online, followed by a retrospective review of detailed medical records of potential cases. Dogs were included if episodes consistent with cataplexy were present during examination by a board-certified veterinary neurologist and diagnostic work-up included magnetic resonance imaging of the brain and analysis of cerebrospinal fluid.

Results: Seven French Bulldogs and 1 Chihuahua (age range, 9-66 months) were included. Meningoencephalitis of unknown origin was diagnosed in 2 dogs, extracranial foci of inflammation were identified in 2 dogs (aspiration pneumonia, esophagitis, otitis media), and no abnormalities were found on diagnostic investigations in 4 dogs. Prednisolone was used in the management of all dogs, 6 dogs received imipramine, and 2 received cytosine arabinoside. An initial remission of signs was observed in all dogs, but a subsequent relapse of clinical signs was recorded for 4 dogs, of which 3 responded to adjustment or resumption of treatment.

Conclusions and Clinical Importance: The presence of cataplexy episodes should prompt a thorough diagnostic work-up to exclude the presence of intracranial (and extracranial) pathology. The potential for both remission and relapse of signs in suspected acquired cases is important for clinicians and owners to be aware of.

KEYWORDS

French Bulldog, hypocretin, meningoencephalitis, sleep disorder, symptomatic narcolepsy

1 | INTRODUCTION

Narcolepsy is a sleep disorder characterized by hypersomnia (ie, excessive sleepiness) and is often associated with cataplexy.[1-3] The presence of partial or complete cataplexy (sudden onset skeletal muscle atonia) is considered pathognomonic of narcolepsy.[1,4,5]

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; ECVN, European College of Veterinary Neurology; HLA, human leukocyte antigen; MRI, magnetic resonance imaging; MUO, meningoencephalitis of unknown origin; NME, necrotizing meningoencephalitis; NT1, narcolepsy type 1; NT2, narcolepsy type 2; OxR2, hypocretin (orexin) receptor 2 gene; RBC, red blood cell(s); SRMA, steroid responsive meningitis arteritis; SRTS, steroid responsive tremor syndrome; TNCC, total nuclear cell count(s).

Sporadic secondary narcolepsy (also termed "symptomatic" or "acquired" narcolepsy) is characterized by the diagnosis of a concurrent underlying cause for narcolepsy.[1,3] In human medicine, sporadic secondary narcolepsy has been linked to head trauma, tumors, autoimmune disease, encephalitis, and paraneoplastic syndromes.[1,6-9] Sporadic secondary narcolepsy is considered rare, representing <5% of all human narcolepsy cases.[1] In veterinary medicine, the terms "acquired," "secondary," and "symptomatic" have all been used to describe rare cases of narcolepsy with a detectable or suspected underlying cause.[2,10-14] Resolution of clinical signs of acquired narcolepsy is reported in 1 dog with meningoencephalitis of unknown origin (MUO) after treatment with immunosuppressive medication.[12] The aim of this retrospective study was to describe the clinicopathological features and outcome of a larger cohort of dogs with suspected acquired narcolepsy.

2 | MATERIALS AND METHODS

Cases were recruited retrospectively using an online veterinary forum (Veterinary Information Network-VIN American College of Veterinary Internal Medicine-ACVIM/European College of Veterinary Neurology-ECVN Neurologists ListServe) asking international veterinary colleagues to contact us with suspected cases of acquired narcolepsy. Clinical information for each case was retrieved from medical records. Dogs were included if signs of narcolepsy had been present at the time of examination by a board-certified veterinary neurologist, videos of consistent clinical signs such as cataplexy episodes were available for review, and diagnostic work-up included brain magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis. Clinical findings, diagnostic test results, treatments administered, and videos were recorded for each dog. Clinical, telephone, or both clinical and telephone follow-up with the owner of at least 3 months was recorded, and information was obtained on the occurrence of narcoleptic episodes after initiation of treatment.

In all dogs, MRI studies of the brain were performed with 1.5 Tesla MRI-scanners (a, Vantage Elan; Canon Medical Systems, USA; b, Achieva 1.5T, Philips, Best, The Netherlands; c, Intera 1.5T, Philips, Best, The Netherlands; d, 1.5 Tesla Petvet Hallmarq, Surrey, UK), and CSF was collected for analysis from the cisterna magna. Hematological and serum biochemical test results were reviewed with respect to laboratory-specific reference intervals. Supplementary file 1 further details all other diagnostic tests that were performed and recorded for each dog.

3 | RESULTS

3.1 | Animals

Eight dogs were identified from 4 European referral institutions. Seven French Bulldogs (2 male entire, 2 female entire, 2 male neutered, and 1 female neutered) and 1 Chihuahua (male entire), with a median age at diagnosis of 2 years and 3 months (range, 9-66 months) were included. Supplementary file 1 contains information on the clinical presentation, diagnostic test results, clinical diagnosis, treatment, and outcome for each dog. Dogs were presented for various problems, including episodic weakness or collapse (suspected cataplexy, n = 8), lethargy or excessive sleepiness (n = 5), generalized weakness (n = 3), ataxia (n = 3), regurgitation (n = 2), circling (n = 1), head tremor (n = 1), inappetence (n = 1), and progressive obtundation (n = 1). All dogs exhibited episodes of cataplexy as reported by board-certified veterinary neurologists based on witnessed events and review of video material. Seven dogs had an acute onset of clinical signs with progression noted by the owner, referring veterinarian or both, and were presented within 10 days of onset. One dog had a more chronic history of suspected narcolepsy with recent progression. All of the dogs had multiple cataplexy episodes per day, but the daily frequency was variable for each dog and between dogs. These episodes were seen in response to stress, excitement, or other stimuli in all dogs, and in some dogs, the cataplexy events were also seen during walking without witnessed external stimuli. In 5 out of 8 dogs, cataplexy episodes were linked to the dog eating or being offered food. Supplementary file 2 contains a summated video of all included dogs depicting the nature of the observed episodes, provided either by the owners or recorded in the hospital.

3.2 | Clinical examination

Complete clinical examination findings are detailed in Supplementary file 1.

3.2.1 | Neurological examination

In 3 out of 8 dogs, neurological examination was normal other than intermittent episodes of cataplexy during consultation or hospitalization. One dog presented with severe obtundation/stupor, being only responsive to loud noise and noxious stimuli. Lethargy or obtundation (n = 2), cervical hyperesthesia (n = 1), mild ataxia of all limbs (n = 1), circling (n = 1), delayed postural reactions in the pelvic limbs (n = 1), head tilt (n = 1), positional ventrolateral strabismus (n = 1), and reduced menace responses (n = 1) were some of the findings identified on the initial examinations in the remaining 4 dogs. Neurolocalization based on the signs of narcolepsy involved the hypocretinergic system, which is largely based in the brain stem with a particularly important role for the hypothalamus, in all dogs but was thought to be multifocal intracranial for 2 of the dogs.

3.2.2 | Diagnostic tests

Results of hematology, biochemistry, brain MRI, and CSF analysis were available for all dogs (n = 8). One dog had the MRI study extended to include the cervical spinal cord. No definitive cause for the presenting clinical signs was identified on hematology and serum biochemistry in any dog (see Supplementary file 1). Abdominal ultrasound did not reveal

abnormalities in the 2 dogs in which it was performed. Thoracic radiography (n = 3) did not reveal abnormalities in 2 dogs and revealed aspiration pneumonia, a T10 hemivertebra and possible hiatal hernia in 1 dog. Esophagoscopy performed in this dog revealed distal esophagitis and a suspected sliding hiatal hernia. Electrocardiography was performed at the time of cataplectic episodes in 3 dogs, revealing a normal sinus rhythm in 2 dogs and occasional monomorphic premature ventricular complexes in 1 dog. Echocardiography did not reveal abnormalities in the 4 dogs in which it was performed. Serology for *Borrelia burgdorferi*, *Toxoplasma gondii* IgM and IgG, *Neospora caninum*, *Ehrlichia canis*, *Anaplasma canis* (n = 3), and real-time PCR for *Bartonella* spp., *Borrelia burgdorferi* sensu *lato*, Canine distemper virus, *Cryptococcus neoformans*, *Neospora caninum*, and *T gondii* (n = 1) were negative. Comorbidities were identified in 2 out of 8 dogs (esophagitis and aspiration pneumonia (n = 1), and esophagitis, rhinitis, otitis media, keratoconjunctivitis sicca (n = 1)) (see Supplementary file 1).

Magnetic resonance imaging

Brain MRI did not reveal abnormalities in 6 out of 8 dogs, other than various breed-related anatomical changes related to brachycephalic conformation (n = 6) and left-sided otitis media in 1 dog. In the remaining 2 cases, 1 dog had a small, ill-defined focal hyperintensity on fluid-attenuated inversion recovery images in the right parietal lobe and was subsequently diagnosed with MUO based on the analysis of CSF. Brain MRI in the second dog was deemed equivocal because of the finding of multifocal T2W hyperintense regions in the midbrain and brain stem that were only visible in 1 slice orientation.

Cerebrospinal fluid analysis

Cerebrospinal fluid analysis revealed increased total nucleated cell count (TNCC) in 2 dogs, increased RBC in 3 dogs, and increased protein in 1 dog. The median protein concentration was 0.20 g/L (0.14-0.40 g/L), the median TNCC was 3 cells/μL (<2 to 35 cells/μL), the median RBC count was 4 cells/μL (0-1530 cells/μL). In the 2 dogs with increased CSF TNCC, a presumptive diagnosis of MUO was made before initiation of treatment.

3.3 | Treatment

Details on specific treatments for each dog are listed in Supplementary file 1. Extracranial/extraneural comorbidities were treated as deemed necessary. Methylphenidate was used in the treatment of 1 dog by the referring veterinarian, but administration of this medication was stopped because of a lack of response to treatment. Venlafaxine was used in the treatment of 1 dog but was discontinued due to concerns about adverse effects.

3.3.1 | Prednisolone

All dogs received prednisolone at some point in their management. In the 2 dogs that were diagnosed with MUO, treatment with immunosuppressive doses of prednisolone was initiated (2-3 mg/kg PO q24h). In the remaining 6 dogs, treatment with prednisolone (n = 4, circa 2 mg/kg PO q24h) or other immunosuppressive medication (cytosine arabinoside [n = 2], dexamethasone [n = 2]) was started after worsening of clinical signs of narcolepsy despite other medical treatment, spontaneous worsening of narcolepsy without treatment, or worsening of narcolepsy despite therapy for comorbidities. In 1 dog, prednisolone treatment was only initiated after surgical and other medical treatment for otitis media. The prednisolone dosage was anti-inflammatory in that case (0.2 mg/kg PO q24h), before being increased to 2 mg/kg PO q24h 5 months later after worsening of clinical signs of narcolepsy despite imipramine treatment. There was a relapse of clinical signs (narcolepsy) in 3 dogs when the prednisolone dose was tapered, with a subsequent decrease in episode frequency or remission after an increase in dose. The median duration of prednisolone treatment (starting with immunosuppressive doses and gradually tapering) was 155 consecutive days (range, 28-930 days).

3.3.2 | Imipramine

Six of 8 dogs were treated with varying dosages of imipramine at some point in their management (0.45-2.2 mg/kg PO q12h or q8h). In 3 of those dogs, imipramine was added after a partial response to treatment with prednisolone, dexamethasone, cytosine arabinoside, or a combination thereof (reduced frequency of episodes but not complete resolution). A further reduction in episode frequency or severity was reported for all these dogs. In 1 dog, imipramine and prednisolone therapy were started at the same time, and resulted in remission of signs of narcolepsy within 4 days. In the 2 remaining dogs, prednisolone therapy was added after initial therapy with imipramine. In these dogs, subsequent remission of clinical signs was observed on concurrent therapy of prednisolone and imipramine. The median duration of treatment with imipramine was 379 days (range, 35-1095 days).

3.4 | Outcome

In all dogs, the frequency of cataplexy events decreased after initiation of prednisolone therapy, either alone or in combination with other immunosuppressive medication or imipramine. In 3 dogs, the episodes did not recur during treatment with prednisolone nor after tapering of prednisolone (complete remission). These 3 dogs were not receiving any medication at the last follow-up (complete remission without long-term medication). Recurrence or progression of signs was seen in 5 out of 8 dogs. In 4 of these dogs, there was recurrence or worsening of signs after initial partial remission of cataplexy episodes, and in 1 additional dog, central nervous system (CNS) signs of forebrain dysfunction were subsequently observed, which were responsive to immunosuppressive treatment. In the 4 dogs with recurrence of clinical signs, the dosages of prednisolone or imipramine were adjusted, with reduction (n = 1) or remission (n = 3) of the

episodes observed. The 3 dogs that subsequently achieved remission of signs after reintroduction or adjustment of treatment increased the total number of dogs achieving remission in this study to 75% (6 of 8 dogs). In 1 dog, prednisolone therapy was anti-inflammatory at first (0.22 mg/kg PO q12h) with concurrent treatment with imipramine. Five months after presentation, cataplexy episodes worsened again and immunosuppressive dosages of prednisolone were started (2 mg/kg PO q24h) without changing the imipramine dosage. Marked improvement regarding the cataplexy episode frequency was observed after this increase in the prednisolone dose. The median follow-up time for all dogs (from first diagnosis to date of death or last owner contact) was 458 days (range, 180-1095 days). Three dogs were euthanized: at 18 months and 3 years after initial presentation due to non-neurological morbidities in 2 dogs, while 1 dog was euthanized 15 months after initial presentation, reportedly because of signs of neurological disease of a different nature (unspecified paralysis).

4 | DISCUSSION

This retrospective case series describes 8 dogs with suspected acquired narcolepsy in which the clinical signs, most notably cataplexy events, either reduced in frequency or resolved after medical treatment. The terms "symptomatic" and "secondary" narcolepsy have been used in previous single case reports of similar cases.[11-14] The authors prefer to adhere to the term "acquired narcolepsy" as opposed to "symptomatic narcolepsy" or "sporadic secondary narcolepsy" (the latter of which is used in human literature). As a clear genetic form of narcolepsy is lacking in humans,[1] but clearly demonstrated in dogs,[15,16] the term "acquired narcolepsy" seems appropriate to distinguish cases such as reported here from the genetic narcolepsy cases in dogs. The clinical presentation, apparent response to immunosuppressive treatment, and remission of clinical signs seen in several dogs in this study, without specific long-term treatment for narcolepsy, would support the designation as suspected acquired narcolepsy.

There are currently only 4 single case reports of suspected acquired narcolepsy in dogs.[11-14] Three of these discussed in detail here concerned a 10-month-old female entire Argentine Dogo with postvaccinal distemper encephalitis (case A),[11] a 4-year-old female entire Cocker Spaniel with meningoencephalitis of unknown origin (case B),[12] and a 6-year-old male neutered Dachshund with a pituitary macrotumor (case C).[13] Cataplexy was a presenting clinical sign in all cases, triggered by offering food in all 3, as was also the case in 5 out of 8 dogs reported here. In case A, the clinical signs had started at 4 months of age and progressed over the month before presentation. Findings were considered to be suggestive of postvaccinal distemper encephalitis, but the possibility of coincidental encephalitis and sporadic idiopathic narcolepsy could not be ruled out. In the dogs reported here, none had a histopathological confirmation of encephalitis or distemper virus infection, but 2 dogs were diagnosed with presumptive MUO after brain MRI and CSF analysis. Meningoencephalitis of unknown origin was also diagnosed as the cause for an acute onset of narcolepsy, as well as other neurological signs suggestive of a multifocal intracranial localization, in case B. The clinical signs in this case resolved within 3 weeks and no relapse was reported over a total follow-up of 32 months after diagnosis. No symptomatic treatment (eg, imipramine) was used in case B, as for the 2 dogs diagnosed with MUO in this study. In case C, genetic testing was negative for the hypocretin receptor 2 gene mutation reported in the Dachshund and a pituitary macrotumor was diagnosed as the suspected cause for acquired narcolepsy. Genetic testing for this mutation was not performed in this study, as the French Bulldog and Chihuahua are not breeds in which this mutation has been reported. Hypocretin levels in the CSF of case C were determined to be within reference range. Venlafaxine was used in the treatment, but discontinued early on because of side effects, as also reported for the 1 dog in this case series in which it was tried. Gabapentin and prednisolone (0.6 mg/kg PO daily) and stereotactic radiotherapy were also used in the treatment of case C, with continued occasional cataplectic events reported. This is similar to the incomplete remission of clinical signs seen in 2 out of 8 dogs reported in this study. The other remaining case report describes an 8-year-old Boxer with a history of narcolepsy of about 1 year that died because of unrelated issues, suspectedly due a pituitary macrotumor that was found postmortem.[14]

Regarding medical treatment of narcolepsy, imipramine has been reported for treatment of dogs with narcolepsy.[2] Six out of 8 dogs in this study were treated with imipramine at some stage of their treatment. Imipramine can be considered a symptomatic treatment as it does not address an underlying cause.[1,2] Therefore, the administration of imipramine in cases of acquired narcolepsy is similar to the use of antiepileptic drugs in cases of structural epilepsy (such as dogs with MUO or brain neoplasia). Other medications with reported efficacy in human cases of narcolepsy, such as modafinil, methylphenidate, venlafaxine, and antidepressants, are used in dogs.[16-18] Methylphenidate and venlafaxine were implemented in 1 case each reported here, but stopped after questionable efficacy and concerns about side effects.

There is some success of treatment with immunomodulatory medications in human cases of narcolepsy and in dogs with genetic disease.[1,19,20] The reduction in frequency, or complete remission, of narcolepsy after immunosuppressive treatment with corticosteroids (with or without other immunosuppressive medication) in the cases reported here suggests that an underlying cause might have been addressed by these medications. In the cases diagnosed with MUO, this appeared to support an inflammatory process affecting the neuroanatomic structures involved in the regulation of sleep and muscle tone. In the 2 dogs with an acute onset of clinical signs concurrent with an extraneural focus of inflammation (aspiration pneumonia, otitis media), it is possible that the narcolepsy represented a parainfectious (triggered) condition that resolved after management of the concurrent medical condition and the use anti-inflammatory medications. Gross encephalitis as a cause of sporadic secondary narcolepsy in humans is rare.[1,6] The scarcity of reports of acquired cases of narcolepsy in dogs might reflect that this is also the case, as (suspected) immune-mediated meningoencephalitis is a frequently

diagnosed entity in this species.[21,22] In human cases of acute onset narcolepsy, triggering events can be recognized, such as vaccination, viral and bacterial infections, trauma or stress.[1,20] In the remaining dogs in which no specific underlying inflammatory disease was diagnosed, corticosteroids were added to the treatment because of concerns of inflammatory CNS disease despite normal (or equivocal) CSF and MRI findings, and clinical deterioration despite other treatment modalities, in combination with clinical reasoning. The pathophysiology underlying the cases that appeared to respond to immunosuppressive treatment but for which an underlying cause could not be identified remains to be determined. In light of the signalment, clinical signs, and response to immunosuppressive medications in these cases, it remains possible that intraparenchymal brain inflammation (eg, MUO) was present in these cases without being visible on MRI or CSF analysis. The diagnosis of MUO in 2 dogs was based on criteria previously reported and was substantiated by response to immunosuppressive treatment.[21] Imaging abnormalities are present in most cases of MUO, but cases with confirmed MUO might not have visible abnormalities on MRI studies of the brain.[21] It is also possible that the dogs with cisternal CSF TNCC of 0 to 5 cells/μL represented cases of MUO without an increased TNCC (ie, intraparenchymal inflammation without inflammatory cells being present in the CSF at the time of sampling).[22-25] Alternatively, concurrent sampling from the lumbar cistern in addition to the cisternal site may have increased the likelihood of identifying underlying inflammation in these cases.[25]

In human medicine, recent evidence for T-cell autoreactivity has been reported in both NT1 and NT2.[1,26] This, in conjunction with earlier studies, shows a clear association of the prevalence of narcolepsy in humans to genetic factors influencing the human leukocyte antigen (HLA) system and has led to the consensus that an immune-mediated (co-)etiology of narcolepsy is likely to be involved in the pathogenesis.[1,26] A "multiple hit" theory is now generally accepted to explain the still partly elusive pathogenesis of narcolepsy, with genetic predisposition, environmental factors, and triggering events leading to selective immune-mediated damage to neurons in the hypothalamus that are pivotal for the regulation of normal wakefulness and sleep.[1] In human medicine, genotyping of HLA-associated genotypes even plays a role in the diagnosis of narcolepsy. In dogs, the diagnosis of narcolepsy is largely based on clinical observations and, in the genetic form, genetic testing.[2] One study did not find an association between specific dog leukocyte antigen alleles and the development of narcolepsy in familial and sporadic canine cases.[27] In the genetic disease in dogs, there is upregulated major histocompatibility complex class II expression by microglia and there is an effect of immunosuppressive therapy on the onset and severity of clinical signs.[21,28] Bearing this in mind, it could be that there is a role for immunosuppression in the treatment of dogs with acquired narcolepsy and this could explain the apparent response to such treatment shown by a number of the dogs reported in this study.

Our findings provided further support to the suggestion that remission of clinical signs in dogs with suspected acquired narcolepsy can occur.[12,13] Clinical remission or improvement over time occurs in humans.[1] The possibility of remission, and subsequent relapse, of narcolepsy in acquired cases is important for case management and owner discussions. The remission rate in this study eventually reached 75% (6 out of 8 dogs), with 3 dogs showing complete remission without long-term medications. Some dogs achieved remission early in treatment while some never reached complete remission. The possibility of recurrence (relapse), as observed in half of the dogs reported here, is also important to consider and is a feature of other suspected immune-mediated or "steroid responsive" diseases.[29] Clinical follow-up is therefore important in the management of these cases to allow early recognition of a relapse and to adjust treatment when necessary. As more cases are encountered by neurologists, more data will hopefully become available as to the consistency of remission and relapse rates in dogs with acquired narcolepsy.

The French Bulldog was apparently overrepresented in this study, with 7 out of 8 dogs being French Bulldogs. In the previous case report documenting acquired narcolepsy in a dog with underlying MUO, the dog was a Cocker Spaniel.[12] Several other suspected immune-mediated disorders were, at least initially, reported in specific breeds and a predisposition still remains even after documented cases in other breeds. Examples include steroid-responsive meningitis arteritis (SRMA, "beagle pain syndrome"),[29,30] necrotizing meningoencephalitis (NME, "pug dog encephalitis"),[31] and steroid-responsive tremor syndrome (SRTS, "shaker dog syndrome" in the Maltese or "little white shakers").[32,33] A possible predisposition for acquired narcolepsy in French Bulldogs, including those with and those without MUO, needs to be evaluated by future studies.

There are several limitations to this study. Inherent to the experimental design of a retrospective case series, especially when dogs have been presented to multiple facilities, the work-up and treatment of dogs was not standardized. Since a control group is lacking, we cannot state that the treatments employed were responsible for amelioration of clinical signs or that the dogs might have improved without therapy. Therefore, we cannot conclude that the treatment in these dogs was responsible for the partial or complete remission of signs. Another limitation can be found in the large dependence on clinical observations and evaluation of video material for the diagnosis of cataplexy. Cataplexy is pathognomonic for narcolepsy and is characterized by episodes of sudden muscle atonia and areflexia in all limbs and is usually associated with positive emotional stimuli, such as being offered food or eating.[1,2,4] With regard to the dogs included and the videos in Supplementary file 2, other possible causes for the episodes observed or events such as these could include myoclonus or atonic seizures. Recently, epileptic seizures triggered by eating in dogs are also reported.[34] Although atonic seizures in dogs with "eating epilepsy" might be a phenotypical differential diagnosis for cataplexy episodes triggered by eating, atonic seizures have not been reported in this type of reflex seizure in dogs. There are low levels of agreement between veterinary neurology specialists and nonspecialists in the interpretation of videos of canine and feline paroxysmal events.[35] As a result, video footage alone was not an inclusion criterion in this study, with clinical observation of consistent clinical signs during and between episodes by a board-certified diplomate was also required. In addition, the particular episodes seen in the short segments of video

footage in Supplementary file 2 do not cover the whole spectrum of signs seen in the dogs included. Brain activity pattern determination with electroencephalography, together with other diagnostic tests to rule out metabolic disorders, cardiac causes of collapse, and other cataplexy-like episodes, in a more standardized fashion could contribute to the certainty of the diagnosis in future prospective studies.[1-5,12] Physostigmine is used to exacerbate signs in dogs with narcolepsy, but this was not performed in any of the dogs reported here.[2] These options were not feasible in this retrospective study; however, unless the causative gene mutation in dogs is identified, clinical observation of consistent episodes, review of video footage, and the performance of food-elicited cataplexy testing are still the mainstay in the diagnosis of acquired narcolepsy in dogs.[2] Similarly, the definitive diagnosis of narcolepsy in humans is not altogether straightforward and several difficulties are encountered, including recognition of clinical signs and technical difficulties and interpretation of diagnostic tests.[1,2] Finally, caution should be used in interpretation of the results of this study regarding speculation on causal relationships due the low number of dogs included.

In conclusion, the presence of cataplexy episodes should prompt a thorough diagnostic work-up to exclude the presence of intracranial (and extracranial) pathology. The potential for both remission and relapse of signs in suspected acquired cases is important for clinicians and owners to be aware of.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Cefuroxime was used off-label.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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