Received: 22 September 2020 | Accepted: 4 February 2021

DOI: 10.1111/jvim.16068

CASE REPORT

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Levetiracetam-responsive paroxysmal exertional dyskinesia in a Welsh Terrier

Sherril Green[1] | Natasha Olby[2]

[1]Stanford University - Comparative Medicine, Stanford, California

[2]North Carolina State University - College of Veterinary Medicine, Raleigh, North Carolina

Correspondence
Sherril Green, Stanford University - Comparative Medicine, 300 Pasteur Drive, Stanford, CA 94305.
Email: sherril@stanford.edu

Abstract

A 5-and-a-half-year old, 9-kg, spayed, female Welsh Terrier presented with a 12 month history of paroxysmal exertion-induced dyskinesia (PED) characterized by recurrent episodes of involuntary hyperkinetic movements, abnormal muscle tone, and contractions triggered by exercise. A single episode occurred within 2 hours after exercise, lasted from 7 to 10 minutes, and resolved without treatment. The owner sought treatment for the dog when the episodes began to last longer (20-30 minutes), and occurred as long as 2.5 to 8 hours after exercise. Diazepam administered intranasally at the start of an episode promptly alleviated the symptoms. Maintenance therapy with levetiracetam proved effective, such that the dog was gradually returned to exercise. However, attempts to wean the dog off the drug resulted in reoccurrence. Although the pathophysiology of PED is not fully understood, the clinical presentation and the positive response to antiepileptic therapy highlight the overlap between disease pathways in epilepsy and PED in dogs.

KEYWORDS
movement disorder, paroxysmal dyskinesia, treatment, Welsh Terrier

1 | INTRODUCTION

Paroxysmal dyskinesia (PD) refers to a group of movement disorders (MDs) characterized by recurring episodes of involuntary hyperkinetic movements, ballism, dystonia, athetosis, or chorea.[1-3] The irregular muscle movements typically involve the limbs, trunk, neck and/or face, last minutes to several hours, and occur without a loss of consciousness. The PDs have been classified into 3 main types: paroxysmal kinesigenic dyskinesia (PKD), in which an episode is induced by an abrupt, voluntary physical movement; paroxysmal nonkinesigenic dyskinesia, in which episodes are not preceded by sudden movement or exercise; and paroxysmal exertion-induced dyskinesia (PED), in which episodes are triggered by prolonged exercise.[4] The phenomenology overlaps between the PDs and other types of MDs, and because diagnostic tests tend to show no specific abnormalities or are inconclusive, PD classification algorithms have been expanded to include additional triggers (eg, heat, cold, stress, anxiety, caffeine, alcohol, sleep, or waking from sleep), the age of onset, severity of clinical signs, episode frequency and duration, and the presence of coexisting signs (eg, ataxia, hemiplegia, migraines, parkinsonism, or epilepsy).[1,5] Paroxysmal dyskinesias as recognized in human patients might be associated with acquired conditions (eg, metabolic disturbances, toxicosis, or trauma), immune-mediated disorders, vascular or neurodegenerative disorders, idiopathic, or attributed to known or suspected genetic mutations.[1,2,5-24]

The PDs share phenomenology with, and can be difficult to distinguish from, focal epileptic seizures.[1,2,5] Most PD patients have a positive response to antiepileptic medications, suggesting overlap

Abbreviations: AED, antiepileptic drug; CSF, cerebral spinal fluid; EEG, electroencephalography; MD, movement disorder; PD, paroxysmal dyskinesia; PED, paroxysmal exertion-induced dyskinesia.

between the disease pathways. However, consciousness is preserved in PD and electroencephalographic findings in PD patients are normal before, during, and after an episode. Thus, the PDs are considered distinct, nonepileptic disorders.

Movement disorders characterized as PD are increasingly reported in a number of dog breeds, including Cavalier King Charles Spaniels, Scottish Terriers, and Border Terriers, among others.[2,17,25-55]

Therapeutic management strategies for PD in dogs have relied on conventional antiepileptic drugs (AEDs; namely the benzodiazepines) alone, or in combination with carbonic anhydrase inhibitors, muscle relaxants, glucocorticoids and other anti-inflammatory agents, or dietary changes. Levetiracetam, a novel AED which modulates neurotransmitter release by binding to the synaptic vesicle protein SV2A, has been used to treat epilepsy and PD since the early 2000s.[4,5,56] Here, we report PED in a Welsh Terrier and long term management with levetiracetam.

1.1 | Case history

A 5-and-half year old spayed, 9-kg, female Welsh Terrier, presented with a 12-month history of abnormal muscle contractions and "cramping" that occurred after prolonged exercise (within 15-20 minutes after 30 minutes of ball chasing or after hour-long hikes with the owner). The owner reported that initially, a single episode generally lasted from 7 to 10 minutes and resolved without treatment. The owner reported that the dog did not lose consciousness during an episode. The dog experienced cramping that started in a hind limb and progressed to involve all 4 limbs, and the back muscles, such that the dog assumed a stiffened, hunchbacked appearance.

The owner sought treatment for the dog when the episodes began to last longer (20-30 minutes) and occurred repeatedly (2-3 times) over an extended period (2-8 hours) after exercise and were followed by emesis within 1 to 2 hours after the muscle contractions ceased. The dog became increasingly inappetent and lethargic and lost 1.4 kg of body weight over the previous 2 months. The owner ceased exercising the dog, but reported that the dog recently experienced an episode lasting ~20 minutes (Supporting Video S1) that was triggered by a 15 minute walk before a trip to the veterinarians.

All vaccinations were current and the dog was maintained on milbemycin oxime (Trifexis, Elanco, Greenfield, Indiana) to manage external and internal parasites. The dog had been fed a balanced, grain free, gluten free, single source protein diet (Healthy Balance) for the last 3 years. Results from hematological and serum biochemical tests and urinalysis collected on 3 different occasions over the past 6 months, 2 of which had been collected within 20 minutes after an episode, did not reveal any abnormalities.

Evaluation of the video-taped episode revealed after exercise muscle tremors and fasciculation, contractions that usually began in a hind limb. Contractions progressed to involve the other limbs, the epaxial muscles, the trunk, and the neck. The dog assumed a stiffened posture with an arched back and the head in a lowered position. Photographs (Figure 1A,B) show the postural changes observed during the PED episode. During the episodes, the dog also panted, made lip-smacking motions, and sought comfort from the owners. The dog remained alert and responsive to the owners' commands, and did not show altered mentation, or blindness. The episodes were not characterized by a prodrome, ictal, or post ictal behavior. The dog often lay down, but did not collapse or fall over. She remained recumbent until the large-muscle contractions and most of the fine muscle tremors and fasciculation rescinded. Upon cessation of an episode, the dog quickly fully recovered and ambulated normally.

The initial differential diagnoses included Canine Epileptoid Cramping Syndrome, previously known as Spike's disease, as reported in Border Terriers, or a condition similar to Scottie Cramp as seen in Scottish Terriers, or similar to the well-recognized PD known as episodic falling syndrome as described in King Charles Cavalier Spaniels. Epilepsy in dogs was also considered as a differential diagnosis. Upon review of the videos, the dog did not appear to lose consciousness during the episodes and responded to the owners' commands. Given that dystonic episodes were consistently triggered by prolonged exercise and occurred without a loss of consciousness, PED was considered as the working diagnoses.

A treatment regimen was implemented with the goal of mitigating the frequency and duration of the episodes, such that the dog's quality of life could be improved. Therapeutic agents which were safer and with fewer adverse effects were empirically selected. Exercise remained restricted and the dog was initially placed on the short

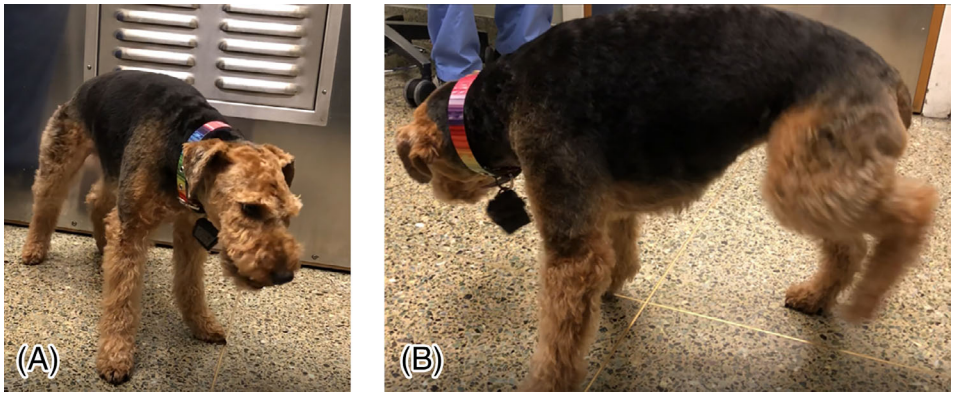

FIGURE 1 A 5-and-a-half year old, 9-kg, female Welsh Terrier with paroxysmal exertion-induced dyskinesia (PED) showing an arched back due to lumbar and thoracic muscle contractions (A) and contraction of the hind limb (B)

acting muscle relaxant methocarbamol (Robaxin, Endo Pharmaceuticals, Malvern, Pennsylvania; starting dosage, 250 mg PO, BID for 2 weeks), and the antiepileptic gabapentin (Neurontin Pfizer, New York, New York; starting dosage, 250 mg PO, BID). The owner slowly reintroduced light exercise (15 minute walks) over the following month and administered 2 mg intranasal diazepam (Diazepam, Hospira Inc, Lake Forest, Illinois), in the event an episode occurred. An antiemetic, maropitant citrate (Cerenia, Zoetis, Kalamazoo, Michigan; starting dosage, 24 mg PO, SID) was also administered to ease after episode vomiting. During this initial 4 week treatment period, the owner observed that treatment with methocarbamol and gabapentin did not prevent the episodes after light exercise. Intranasal diazepam, however, was very effective at stopping the episodes, usually within a minute or less after administration. After treatment with diazepam, the dog was notably sedated and somewhat lethargic. The owner observed that it appeared to be important to interrupt the progression of the episode by immediately administering intranasal diazepam at the onset. If left untreated, the episodes tended to last longer and increase in severity. Because methocarbamol and gabapentin were ineffective, the owner discontinued both medications and placed the dog on levetiracetam (Keppra, UCB, Smyrna, Georgia; 250 mg, PO, TID). After 2 weeks of treatment with levetiracetam, the owner did not observe any episodes, even after moderate exercise (20-30 minute walks). Subsequent genetic testing for mutations in the BCAN[52,53] and *PIGN*[55] gene was performed and was negative.

After 8 months of treatment, the owner attempted to lower the dosage of levetiracetam with the intent to eventually wean the dog off of the medication. Three attempts, 2 weeks apart, to lower the dosage to 125 mg, PO, q8h, resulted in reoccurrence of the PD after light exercise, although the episodes were very mild and short in duration. The dog has since remained on treatment with levetiracetam, 250 mg, PO, q8h, given light exercise (30-60 minutes of walking/day) and allowed short (<10 minutes), infrequent sessions of ball chasing and has had only 1 mild episode in the past 47 months.

2 | DISCUSSION

This is a report of PED in a Welsh Terrier that describes a successful therapeutic approach to the long-term management using the novel AED levetiracetam. Although the findings reported here must be interpreted within the limitations of a single case, the incidence of PED in Welsh Terriers is currently unknown. However, it is difficult to diagnose and therefore might be underreported. It is unknown if other members of this Welsh Terrier's pedigree are affected.

The phenomenology in this Welsh Terrier overlaps with PD disorders in other dog breeds. Paroxysmal dyskinesia in Border Terriers is also characterized by recurrent episodes of abnormal involuntary muscle movements, with no loss of consciousness.[31,32,57] However, the episodes were not preceded by prolonged exercise, and were triggered by waking from sleep or by excitement. Approximately ~20% to 30% of affected Border Terriers display autonomic signs (borborygmi, urination, and diarrhea).[57] Various treatments had variable-to-good outcomes over the short term, including the administration of conventional AEDs.[57] Switching affected dogs to a gluten-free diet, in conjunction with pharmaceutical therapeutics, reportedly ameliorated the clinical signs.[58] Although the Welsh Terrier described here displayed similar PD signs, a consistent trigger for this dog was prolonged exercise. The dog in this report sometimes experienced emesis after episode, but other autonomic signs were not present. The dog in this report had been on gluten-free diet for 3 years prior to the diagnosis and had experienced PED during that time, suggesting that a gluten-free diet did not have an impact on the condition. Notably, switching to a ketogenic diet ameliorates the symptoms in some human patients with PD.[1] This effect may be related to an alternate energy source in the food, rather than antiepileptic properties of the diet, per se. Feeding a ketogenic diet was not attempted in the dog described in this report.

Comparatively, the PD phenomenology in this Welsh Terrier shares more overlapping features with those seen in Scottish Terriers[17,34-36,40,44,59,60] with Scottie Cramp and with those as reported in King Cavalier Charles Spaniels[28,30,42,46,50] with PD, including: exercise as a trigger, episodes that involved increasing muscle tone and stiffness of the extremities, postural arching of the back, no loss of consciousness, and responsiveness to treatment with conventional antiepileptic medications. The Welsh Terrier described here did not however, collapse or fall over, or assume a "praying position" during a PD episode (as described in King Cavalier Charles Spaniels) or fall or summersault when running, or collapse during exercise and recover in a few minutes, only to collapse and recover again after continuing to exercise as observed in Scottish Terriers with Scottie Cramp.[44,59]

Epilepsy in dogs was also considered as a differential diagnosis in the dog described in this report, but distinguishing PD in dogs from an epileptic disorder poses a particular diagnostic challenge. An increased ratio of cerebral spinal fluid (CSF)/serum glucose is a useful diagnostic tool in human PED, and the electroencephalography (EEG) indices in human medicine are helpful in ruling out seizure disorders, but CSF/serum glucose ratios in PDs in dogs are not described and EEG indices in epilepsy in dogs are not as well characterized.[60-62] Assessing loss of consciousness or impairment of consciousness in epilepsy of dogs is an added challenge, as the EEG indices in dogs have not been well-established.[62] Conscious impairment in dogs is generally assessed subjectively, by evaluating the dog's ability to respond to owners' commands.[49] The Welsh Terrier described here does not appear to lose consciousness or experience conscious impairment. She readily responds to the owners' command to "come here." Other tests that have the potential to clarify the antemortem diagnosis, such as muscle biopsies, computerized tomography, or magnetic resonance imaging of the brain can be cost prohibitive or impractical in veterinary medicine and might not provide additional diagnostic information regarding the PDs.[1,5,60,61] Although this dog tested negatively for mutations for the BCAN and *PIGN* gene, mutations reported to cause PD in Cavalier King Charles Spaniels and Soft-Coated Wheaten Terriers, respectively, tests developed for 1 breed may produce falsely negative results if the new breed has a different mutation.

Antiepileptic drugs as first-line therapeutics for the PD, especially for the PKDs, are reported to be effective in human patients and are often given in combination with other medications.[5] The muscle

relaxant methocarbamol and the AED gabapentin, both of which are considered relatively safe and have minimal adverse effects, did not ameliorate the PED in this Welsh Terrier. However, diazepam, a benzodiazepine and GABA agonist, when administered intranasally immediately at the start of an episode, effectively halted the dog's PD. Levetiracetam alone was highly effective in controlling this dog's PED over the long term, such that the dog was able to return to exercise. There are reports that PD might be self-limiting in humans and in dogs.[49,53,58] However, attempts to wean the dog described in this report off of the medication resulted in reoccurrence of disease.

The use of levetiracetam for the treatment of epilepsy and of PD in humans is well documented.[56] It offers the pharmacokinetic advantages of rapid and near complete absorption when given orally, the absence of interactions with other drugs, the absence of enzyme induction and insignificant binding to plasma protein, among others.[56] Levetiracetam was efficacious in the treatment of PED in this dog, and there were no long-term adverse effects after 47 months. It remains unclear how levetiracetam acts specifically to control or ameliorate the symptoms of PD, although modulation of the synaptic neurotransmitter release in the brain probably plays a role. The animal's response to these 2 AEDs, diazepam in the short term and levetiracetam thereafter, further supports the tenet that epilepsy and PD share pathophysiological pathways.

ACKNOWLEDGMENT

No funding was received for this study.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

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.

ORCID

Sherril Green https://orcid.org/0000-0003-0086-2391
Natasha Olby https://orcid.org/0000-0003-1349-3484

REFERENCES

1. Erro R, Bhatia KP. Unravelling of the paroxysmal dyskinesias. *J Neurol Neurosur Psychiatr*. 2019;90(2):227-234.
2. Erro R, Bhatia KP, Espay AJ, Striano P. The epileptic and nonepileptic spectrum of paroxysmal dyskinesias: channelopathies, synaptopathies, and transportopathies. *Mov Disord*. 2017;32(3):310-318. https://doi.org/10.1002/mds.26901.
3. Erro R, Stamelou M, Bhatia KP. Paroxysmal dyskinesias. In: Jankovic J, Toloso E, eds., *Parkinson's Disease and Movement Disorders*. 6th ed. Philadelphia, PA: Lippincot Williams & Wilkins; 2015:397-404.
4. Demirkiran M, Jankovic J. Paroxysmal dyskinesias: clinical features and classification. *Ann Neurol*. 1995;38(4):571-579. https://doi.org/10.1002/ana.410380405.
5. Freitas ME, Ruiz-Lopez M, Dalmau J, et al. Seizures and movement disorders: phenomenology, diagnostic challenges and therapeutic approaches. *J Neurol Neurosurg Psychiatr*. 2019;90(8):920-928.
6. Chen W-J, Lin Y, Xiong Z-Q, et al. Exome sequencing identifies truncating mutations in PRRT2 that cause paroxysmal kinesigenic dyskinesia. *Nature Genet*. 2011;43(12):1252-1255.
7. De Giorgis V, Veggiotti P. GLUT1 deficiency syndrome 2013: current state of the art. *Seizure*. 2013;22(10):803-811.
8. Du W, Bautista JF, Yang H, et al. Calcium-sensitive potassium channelopathy in human epilepsy and paroxysmal movement disorder. *Nat Genet*. 2005;37(7):733-738.
9. Ebrahimi-Fakhari D, Saffari A, Westenberger A, Klein C. The evolving spectrum of PRRT2-associated paroxysmal diseases. *Brain*. 2015;138(12):3476-3495.
10. Erro R, Sheerin UM, Bhatia KP. Paroxysmal dyskinesias revisited: a review of 500 genetically proven cases and a new classification. *Mov Disord*. 2014;29(9):1108-1116.
11. Gardella E, Becker F, Møller RS, et al. Benign infantile seizures and paroxysmal dyskinesia caused by an SCN8A mutation. *Ann Neurol*. 2016;79(3):428-436.
12. Gardiner AR, Jaffer F, Dale RC, et al. The clinical and genetic heterogeneity of paroxysmal dyskinesias. *Brain*. 2015;138(12):3567-3580.
13. Lee H-Y, Huang Y, Bruneau N, et al. Mutations in the gene PRRT2 cause paroxysmal kinesigenic dyskinesia with infantile convulsions. *Cell Rep*. 2012;1(1):2-12.
14. Lee H-Y, Xu Y, Huang Y, et al. The gene for paroxysmal non-kinesigenic dyskinesia encodes an enzyme in a stress response pathway. *Hum Mol Genet*. 2004;13(24):3161-3170.
15. Li J, Zhu X, Wang X, et al. Targeted genomic sequencing identifies PRRT2 mutations as a cause of paroxysmal kinesigenic choreoathetosis. *J Med Genet*. 2012;49(2):76-78.
16. Méneret A, Grabli D, Depienne C, et al. PRRT2 mutations: a major cause of paroxysmal kinesigenic dyskinesia in the European population. *Neurol*. 2012;79(2):170-174.
17. Meyers KM, Padgett GA, Dickson WM. The genetic basis of a kinetic disorder of Scottish terrier dogs. *J Hered*. 1970;61(5):189-192. https://doi.org/10.1093/oxfordjournals.jhered.a108080.
18. Nobile C, Striano P. PRRT2: a major cause of infantile epilepsy and other paroxysmal disorders of childhood. *Prog Brain Res*. 2014;213:141-158. https://doi.org/10.1016/b978-0-444-63326-2.00008-9.
19. Rainier S, Thomas D, Tokarz D, et al. Myofibrillogenesis regulator 1 gene mutations cause paroxysmal dystonic choreoathetosis. *Arch Neurol*. 2004;61(7):1025-1029.
20. Schneider SA, Paisan-Ruiz C, Garcia-Gorostiaga I, et al. GLUT1 gene mutations cause sporadic paroxysmal exercise-induced dyskinesias. *Mov Disord*. 2009;24(11):1684-1688.
21. Suls A, Dedeken P, Goffin K, et al. Paroxysmal exercise-induced dyskinesia and epilepsy is due to mutations in SLC2A1, encoding the glucose transporter GLUT1. *Brain*. 2008;131(7):1831-1844.
22. Wang K, Zhao X, Du Y, et al. Phenotypic overlap among paroxysmal dyskinesia subtypes: Lesson from a family with PRRT2 gene mutation. *Brain Dev*. 2013;35(7):664-666.
23. Weber YG, Storch A, Wuttke TV, et al. GLUT1 mutations are a cause of paroxysmal exertion-induced dyskinesias and induce hemolytic anemia by a cation leak. *J Clin Invest*. 2008;118(6):2157-2168.
24. Zhang ZB, Tian MQ, Gao K, Jiang YW, Wu Y. De novo KCNMA1 mutations in children with early-onset paroxysmal dyskinesia and developmental delay. *Mov Disord*. 2015;30(9):1290-1292.
25. Black V, Garosi L, Lowrie M, Harvey RJ, Gale J. Phenotypic characterisation of canine epileptoid cramping syndrome in the Border terrier. *J Small Anim Pract*. 2014;55(2):102-107. https://doi.org/10.1111/jsap.12170.

26. De Risio L, Freeman J. Epileptoid cramping syndrome in the Norwich Terrier: clinical characterisation and prevalence in the UK. Proceedings 28th Symposium ESVN-ECVN 2015; Amsterdam, the Netherlands.
27. Gill JL, Capper D, Vanbellinghen J-F, et al. Startle disease in Irish wolfhounds associated with a microdeletion in the glycine transporter GlyT2 gene. *Neurobiol Dis*. 2011;43(1):184-189.
28. Garosi LS, Platt SR, Shelton GD. Hypertonicity in Cavalier King Charles spaniels. *J Vet Int Med*. 2002;16:186-187.
29. Harcourt-Brown T. Anticonvulsant responsive, episodic movement disorder in a German shorthaired pointer. *J Small Anim Pract*. 2008;49(8):405-407.
30. Herrtage ME, Palmer AC. Episodic falling in the cavalier King Charles spaniel. *Vet Rec*. 1983;112:458-459.
31. Kloene J, Sewell AC, Hamann H, et al. Klinische Untersuchungen zu Krampfanfällen bei Border Terriern. *Kleintierpraxis*. 2008;53:5-12.
32. Lowrie M, Garden O, Hadjivassiliou M, et al. The clinical and serological effect of a gluten-free diet in border terriers with epileptoid cramping syndrome. *J Vet Int Med*. 2015;29(6):1564-1568.
33. Martlé V, Bhatti S, O'Brien D, et al. Paroxysmal dyskinesia in adult Maltese dogs? Proceedings 28th Annual symposium ESVN-ECVN; 2015. Amsterdam, the Netherlands.
34. Meyers K, Lund J, Padgett G, et al. Hyperkinetic episodes in Scottish Terrier dogs. *J Am Vet Med Assoc*. 1969;155(2):129-133.
35. Meyers KM, Dickson WM, Lund JE, Padgett GA. Muscular hypertonicity: episodes in Scottish Terrier dogs. *Arch Neurol*. 1971;25(1):61-68.
36. Meyers KM, Dickson WM, Schaub RG. Serotonin involvement in a motor disorder of Scottish terrier dogs. *Life Sci*. 1973;13(9):1261-1274.
37. Packer R, Patterson E, Taylor J, et al. Characterization and mode of inheritance of a paroxysmal dyskinesia in Chinook dogs. *J Vet Int Med*. 2010;24(6):1305-1313.
38. Park H-J, Seo D-K, Song K-H, et al. Paroxysmal dyskinesia suspected as canine epileptoid cramping syndrome in a young Yorkshire terrier dog. *J Vet Med Sci*. 2014;76(8):1129-1132.
39. Penderis J, Franklin RJM. Dyskinesia in an adult bichon frise. *J Small Anim Pract*. 2001;42(1):24-25.
40. Peters RI Jr, Meyers KM. Precursor regulation of serotonergic neuronal function in Scottish Terrier dogs 1. *J Neurochem*. 1977;29(4):753-755.
41. Ramsey IK, Chandler KE, Franklin RJM. A movement disorder in boxer pups. *Vet Rec*. 1999;144(7):179-180.
42. Rusbridge C. Neurological diseases of the Cavalier King Charles spaniel. *J Small Anim Pract*. 2005;46(6):265-272.
43. Shelton GD. Muscle pain, cramps and hypertonicity. *Vet Clinics NA: Sm Animl Pract*. 2004;34(6):1483-1496.
44. Urkasemsin G, Olby N. Clinical characteristics of Scottie Cramp in 31 cases. *J Small Animal Pract*. 2015;56(4):276-280.
45. Woods C. Hyperkinetic episodes in two Dalmation dogs [Abnormal increases in motor function, Scotty cramp]. *J Am Anim Hosp Assoc (USA)*. 1977;13:255-257.
46. Wright JA, Smyth J, Brownlie SE, et al. A myopathy associated with muscle hypertonicity in the Cavalier King Charles Spaniel. *J Comp Pathol*. 1987;97(5):559-565.
47. Garosi L, Harvey RJ. Scottie cramp and canine epileptoid cramping syndrome in Border terriers. *Vet Rec*. 2012;170(7):186-187. https://doi.org/10.1136/vr.e1127.
48. Geiger KM, Klopp LS. Use of a selective serotonin reuptake inhibitor for treatment of episodes of hypertonia and kyphosis in a young adult Scottish Terrier. *J Am Vet Med Assoc*. 2009;235(2):168-171. https://doi.org/10.2460/javma.235.2.168.
49. Richter A, Hamann M, Wissel J, Volk HA. Dystonia and paroxysmal dyskinesias: under-recognized movement disorders in domestic animals? A comparison with human dystonia/paroxysmal dyskinesias. *Front Vet Sci*. 2015;2(65):1-14. https://doi.org/10.3389/fvets.2015.00065.
50. Wright JA, Brownlie SE, Smyth JB, Jones D, Wotton P. Muscle hypertonicity in the cavalier King Charles spaniel—myopathic features. *Vet Rec*. 1986;118(18):511-512. https://doi.org/10.1136/vr.118.18.511.
51. Polidoro D, Van Ham L, Santens P, et al. Phenotypic characterization of paroxysmal dyskinesia in Maltese dogs. *J Vet Intern Med*. 2020;34(4):1541-1546. https://doi.org/10.1111/jvim.15804.
52. Forman OP, Penderis J, Hartley C, Hayward LJ, Ricketts SL, Mellersh CS. Parallel mapping and simultaneous sequencing reveals deletions in BCAN and FAM83H associated with discrete inherited disorders in a domestic dog breed. *PLoS Genet*. 2012;8(1):e1002462.
53. Gill JL, Tsai KL, Krey C, et al. A canine BCAN microdeletion associated with episodic falling syndrome. *Neurobiol Dis*. 2012;45(1):130-136.
54. Nessler J, Hug P, Mandigers PJJ, et al. Mitochondrial PCK2 missense variant in Shetland sheepdogs with paroxysmal exercise-induced dyskinesia (PED). *Genes (Basel)*. 2020;11(7):1-14. https://doi.org/10.3390/genes11070774.
55. Kolicheski AL, Johnson GS, Mhlanga-Mutangadura T, et al. A homozygous PIGN missense mutation in Soft-Coated Wheaten Terriers with a canine paroxysmal dyskinesia. *Neurogenetics*. 2017;18(1):39-47. https://doi.org/10.1007/s10048-016-0502-4.
56. Abou-Khalil B. Levetiracetam in the treatment of epilepsy. *Neuropsychiatr Dis Treat*. 2008;4(3):507-523. https://doi.org/10.2147/ndt.s2937.
57. Stassen QEM, Koskinen LLE, van Steenbeek FG, et al. Paroxysmal Dyskinesia in Border Terriers: Clinical, Epidemiological, and Genetic Investigations. *J Vet Intern Med*. 2017;31(4):1123-1131. https://doi.org/10.1111/jvim.14731.
58. Lowrie M, Garden O, Hadjivassiliou M, et al. Canine epileptoid cramping syndrome: a gluten sensitive paroxysmal movement disorder–more than a gut feeling. Paper presented at: Proceedings 28th ESVN-ECVN Congress; 2015; Amsterdam. p. 42.
59. Clemmons R, Peters R, Meyers K. Scotty cramp: a review of cause, characteristics, diagnosis, and treatment. *Compend Contin Educ Pract Vet*. 1980;2:385-388.
60. Jankovic J, Demirkiran M. Classification of paroxysmal dyskinesias and ataxias. *Adv Neurol*. 2002;89:387-400.
61. Erro R, Stamelou M, Ganos C, et al. The clinical syndrome of paroxysmal exercise-induced dystonia: diagnostic outcomes and an algorithm. *Mov Disord Clin Prac*. 2014;1(1):57-61.
62. Berendt M, Farquhar RG, Mandigers PJ, et al. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals. *BMC Vet Res*. 2015;11(1):182.

SUPPORTING INFORMATION

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

How to cite this article: Green S, Olby N. Levetiracetam-responsive paroxysmal exertional dyskinesia in a Welsh Terrier. *J Vet Intern Med*. 2021;35:1093–1097. https://doi.org/10.1111/jvim.16068