Case Series

jfms Journal of Feline Medicine and Surgery

Neurogenic urinary retention in cats following severe cluster seizures

Journal of Feline Medicine and Surgery
1–5

DOI: 10.1177/1098612X15602739
jfms.com
SAGE

Federica Balducci[1], Luisa De Risio[2], Anita Shea[2], Sara Canal[1,3], Fabio Stabile[2] and Marco Bernardini[1,3]

Abstract

Case series summary Four cats that presented with severe cluster seizures developed neurogenic urinary retention in the postictal phase. None of the cats had previous seizures. Micturition was reported as normal in all cats for 3 or more years before seizure onset. All cats required a continuous rate infusion of propofol to control the seizure activity. In all cats manual bladder expression was performed every 8 h until recovery of normal micturition. One cat was started on phenoxybenzamine to reduce internal urethral sphincter tone. All cats recovered normal micturition within 4 weeks of the end of cluster seizures.

Relevance and novel information Transient neurogenic urinary retention has not previously been reported in dogs and cats following severe cluster seizures. Urinary retention should be considered a potential postictal deficit, promptly recognised and treated to avoid urinary tract infection and detrusor muscle atony.

Accepted: 31 July 2015

Introduction

Neurogenic urinary retention has not previously been reported in cats following severe seizure activity. We describe four cats that presented at two referral institutions with severe cluster seizures and that subsequently developed the inability to urinate despite a normal urinary system and no evidence of either brain stem or spinal cord dysfunction.

Cat 1

A 4-year-old female spayed domestic shorthair (DSH) indoor cat presented with a 6 day history of severe clusters of focal motor and autonomic, and focal complex secondarily generalised seizures. There was no prior history of seizures. No urinary system or micturition disorders were reported prior to seizure onset. Exposure to toxins was unlikely.

Treatment with phenobarbital (Luminale, 5 mg/kg PO q12h; Bracco) was started in the previous 48 h without significant improvement. Prereferral complete blood count (CBC) and serum biochemistry results were unremarkable; feline immunodeficiency virus (FIV)/feline leukaemia virus (FeLV) testing was negative (IDEXX SNAP Combo Plus Test). General physical examination was normal. The neurological examination was conducted in the postictal phase and revealed obtunded mentation and reduced menace responses bilaterally. The remainder of the neurological examination was normal. Magnetic resonance imaging (MRI; 0.22T MrV [Paramed]) of the head revealed bilaterally symmetrical increased signal intensity compared with normal grey matter on T2-weighted (T2W) and fluid attenuation inversion recovery (FLAIR) images in the hippocampi and piriform lobes. The lesions were isointense in T1-weighted (T1W) images and markedly and homogeneously enhanced after gadolinium (Dotarem, gadoteric acid 0.5 mmol/ml; Guerbet) administration. Cerebellomedullary cistern cerebrospinal fluid (CSF) analysis was unremarkable. Differential diagnoses included epilepsy of unknown origin with postictal MRI changes and feline hippocampal necrosis (FHN).[1,2]

Owing to the persistence of cluster seizures despite treatment with phenobarbital and diazepam (Valium, 0.5 mg/kg IV; Roche), the cat required a continuous rate

[1]Neurology Unit, Portoni Rossi Veterinary Hospital, Zola Predosa, Bologna, Italy
[2]Neurology/Neurosurgery Service, Centre for Small Animal Studies, Animal Health Trust, Newmarket, UK
[3]Department of Animal Medicine, Production and Health, Clinical Section, University of Padua, Legnaro, Padua, Italy

Corresponding author:
Federica Balducci DVM, Neurology Unit, Portoni Rossi Veterinary Hospital, Via Roma 57/A, 40069 Zola Predosa, Italy
Email: federica.balducci@portonirossi.it

infusion (CRI) of propofol (Rapinovet, 0.1–0.6 mg/kg/min IV; Bayer) over a 12 h period to control seizure activity. During sedation the cat received intravenous fluids at maintenance rate, and the urinary bladder was palpated and expressed every 6 h. After discontinuation of the propofol infusion, the cat was able to ambulate in its cage, but was not witnessed to use the litter tray or to posture to urinate. However, patches of urine in the bedding were noticed during hospitalisation. After a seizure-free period of 48 h the neurological examination was normal and the cat was discharged on phenobarbital (2.5 mg/kg PO q12h).

Abnormal toileting behaviour and lack of voluntary micturition was reported by the owner over the following 36 h. At that stage the referring veterinary surgeon noticed a distended urinary bladder. The cat was easily catheterised and urinalysis was normal. Owing to persistent urinary retention, 24 h later the cat underwent a second neurological examination that revealed only a distended urinary bladder that was relatively easy to void through continuous manual expression. The cat was discharged on the same day with the recommendation of manual expression of the urinary bladder every 8 h. The owner was instructed on how to perform manual expression and to seek veterinary help in case of difficulties.

Over the following 3 weeks, progressive improvement leading to voluntary bladder voiding with normal toileting behaviour manifested once a day was reported. The cat continued to have focal-onset epileptic seizures every 2 months, characterised only by vocalisation and aggressive behaviour lasting for seconds. A suggested second MRI study to confirm the diagnosis of FHN was declined by the owner. No further epileptic seizure activity or micturition dysfunction was witnessed until the cat's death for unknown reasons 9 months later.

Cat 2

A 5-year-old female spayed DSH indoor cat presented for a severe cluster of focal motor and autonomic, and focal complex secondarily generalised seizures over the previous 24 h. There was no history of seizures prior to this cluster; however, the cat had displayed episodes of aimless vocalisation 10 days earlier. No urinary system or micturition disorders were reported prior to seizure onset. Exposure to toxins was unlikely.

Prereferral CBC and serum biochemistry were normal. FIV/FeLV testing was negative. General physical and neurological examinations were normal. MRI (0.22T MrV; Paramed) of the head revealed moderate symmetrical hyperintensity on T2W and FLAIR images of the hippocampi and the piriform lobes, with no abnormalities on pre- and postcontrast T1W images or mass effect. Cerebellomedullary cistern CSF analysis revealed no abnormalities. A diagnosis of epilepsy of unknown origin with MRI postictal changes was made.

During hospitalisation the cat continued to have focal seizures approximately every 2–3 h despite treatment with phenobarbital (2 mg/kg PO q12h) and diazepam (0.5 mg/kg IV). The cat required a CRI of propofol (0.1–0.6 mg/kg/min intravenous) over a 12 h period to control seizure activity. During sedation the cat received intravenous fluids at maintenance rate, and the urinary bladder was palpated and expressed every 6 h. Over the next 12 h two focal-onset epileptic seizures, consisting of contraction of facial muscles, bilateral mydriasis, hypersalivation, vocalisations and alteration of consciousness, were treated with levetiracetam (Keppra, 30 mg/kg IV; UCB Pharma). Following recovery from narcosis, the cat had a normal neurological examination, except for a mildly obtunded mental status, which was attributed to the antiepileptic therapy. However, the cat displayed abnormal toileting behaviour with no interest in the litter tray, it did not posture to urinate and there was a lack of voluntary micturition, and so required manual bladder expression every 8 h.

The cat was discharged on phenobarbital (2 mg/kg PO q12h) 36 h after the last seizure. At home, the owner reported the same abnormal toileting behaviour observed during hospitalisation and bladder expression was necessary. The cat gradually improved and showed voluntary micturition 16 days after discharge. No further epileptic seizure activity or micturition dysfunction was witnessed during a follow-up period of 6 months.

Cat 3

A 6-year-old male neutered DSH indoor cat presented for a severe cluster of focal motor and autonomic, and focal complex secondarily generalised seizures over the previous 2 days. The cat had a history of urethral obstruction due to urinary bladder stones, which had been treated by urethrostomy 3 years earlier. Micturition had been normal following the urethrostomy. Exposure to toxins was unlikely.

Prereferral CBC, biochemistry profile and urinalysis were normal. FIV/FeLV testing was negative. General physical and neurological examinations were unremarkable. MRI (0.22T MrV; Paramed) of the head revealed moderate, symmetrical hyperintensity on T2W and FLAIR images of the hippocampi and the piriform lobes, without mass effect or any abnormalities on pre- and postcontrast T1W images. Cerebellomedullary cistern CSF analysis was within normal limits. A diagnosis of epilepsy of unknown origin with MRI postictal changes was made.

During hospitalisation the cat continued to have focal motor and autonomic, and tonic–clonic generalised seizures approximately every 3 h, despite treatment with phenobarbital (2 mg/kg PO q12h), diazepam (0.5 mg/kg IV) and levetiracetam (30 mg/kg IV). The cat required a propofol CRI over a 24 h period to control seizure activity. During sedation the cat received intravenous

fluids at maintenance rate, and the urinary bladder was palpated and expressed every 6 h. The cat consistently demonstrated a normal physical and neurological examination over the following 24–36 h except for micturition. The bladder was manually expressed every 8 h and the cat was discharged on phenobarbital (2 mg/kg PO q12h) 48 h after the last seizure.

The owner reported that at home the cat showed no interest in the litter tray, it did not posture to urinate and there was a lack of voluntary micturition. Over the following 4 weeks the bladder had to be expressed every 8 h before the cat progressively improved to a normal toileting behaviour. The cat showed focal-onset seizures once a month over a follow-up period of 13 months. No further cluster seizures or micturition dysfunction were witnessed in the same period.

Cat 4

A 12-year-old male neutered DSH cat presented for a severe cluster of focal motor and generalised seizures over the preceding 36 h. There was no history of previous seizures or micturition dysfunction, and exposure to toxins was unlikely.

General physical examination was unremarkable. During the neurological examination, three focal-onset seizures lasting 30–40 s were witnessed, each consisting of fine head and facial twitches, bilaterally dilated and symmetrical pupils, hypersalivation, and loss of response to external stimuli, with several vocalisations preceding return to normal mentation. Between seizures the cat was mentally alert and responsive, with normal posture and gait. Proprioceptive paw placement and hopping were normal in the thoracic limbs but slightly delayed in both pelvic limbs. Spinal reflexes and cranial nerve function were normal. CBC and biochemistry profiles revealed no significant abnormalities. Tests for FIV, FeLV and *Toxoplasma gondii* were all negative. MRI (1.5T Sigma; General Electric Medical System) of the head and cerebellomedullary cistern CSF analysis were unremarkable. A diagnosis of epilepsy of unknown origin was made.

During hospitalisation the cat continued to display focal seizures approximately every hour, despite initiation of treatment with phenobarbital (Epiphen, 2 mg/kg PO q12h; Vétoquinol) and midazolam (Hypnovel, 0.3mg/kg IV; Roche). The cat required a CRI of propofol (0.1–0.6 mg/kg/min IV) over a 24 h period to control seizure activity. During sedation the cat received IV fluids at maintenance rate, and the urinary bladder was palpated and expressed every 6 h. Approximately 24 h following cessation of seizure activity the cat developed pyrexia. A repeated CBC, urinalysis (including culture and sensitivity) and thoracic and abdominal imaging did not reveal any abnormalities. A gallop rhythm on cardiac auscultation was noted to have developed, and echocardiography revealed changes consistent with hypertrophic cardiomyopathy.

The cat was discharged after being seizure free for 48 h. Its body temperature and neurological examinations were normal, and the owner was instructed to administer phenobarbital (2 mg/kg PO q12h), levetiracetam (20 mg/kg PO q8h) and propanolol (Propranolol, 0.33mg/kg PO q12h; Actavis). During hospitalisation large patches of urine were found on the bedding; however, the cat was not seen to use the litter tray, to take the position to urinate or to cover the urine. Following discharge the owner reported signs consistent with overflow incontinence and constipation, with no effort being made to posture to toilet. The cat was catheterised and treated with lactulose, without improvement of toileting behaviour. Owing to persistent urinary retention the cat was readmitted to the referral hospital. Neurological examination revealed a moderately full urinary bladder with some resistance to expression as the sole abnormality. A repeated CBC and urinalysis revealed no significant abnormalities. Treatment with phenoxybenzamine (Dibenyline, 0.5 mg/kg PO q12h; Goldshield) was initiated and the urinary bladder was expressed manually every 8 h. The cat was discharged 11 days later with the recommendation to express the urinary bladder manually every 8 h. The cat progressively improved and normal toileting behaviour was reported by the owner over the following 3 weeks. The cat continued to experience focal and generalised epileptic seizures every 3–4 months. The cat was euthanased 3 years later owing to acute haematemesis, haematochezia, haematuria and epistaxis. Clotting disorders or toxin exposure were the main differential diagnoses of the primary veterinary practitioner.

Discussion

The four cats described in this report all presented for severe cluster seizures and subsequently developed abnormal toileting behaviour characterised by lack of interest in the use of the litter tray, lack of voluntary micturition and urinary retention.[3] In three cats the most likely diagnosis for seizure activity was epilepsy of unknown origin. In one cat, on the basis of MRI findings, FHN was strongly suspected.[1,2]

Micturition includes control of both the storage and evacuation of urine.[4] Normal bladder and urethral anatomy and function are required for micturition to occur. Micturition disorders characterised by urinary retention can result from neurogenic or non-neurogenic causes.[5]

Non-neurogenic urinary retention involves anatomic urethral outflow obstruction.[4] In cats, causes of urethral obstruction are urethral plugs, idiopathic disease, urolithiasis with and without urinary tract infections, urethral spasm and, rarely, stricture and neoplasia.[6] In these cases, urethral catheterisation is often difficult.[4] Moreover, non-neurogenic bladder atony from overdistension, secondary to disruption of the tight junctions of the detrusor myofibres, can lead to failure to eliminate urine.[4]

In our cat population, causes of non-neurogenic urinary retention were unlikely. Indeed, there was no history of urinary tract disease in three cats, and case 3 had normal micturition for 3 years following perineal urethrostomy. Urinalysis was unremarkable in three cats, and no macroscopic changes were noticed in the urine of case 2. In all cats urethral obstruction was unlikely given the ease of both manual expression and catheterisation of the urinary bladder. Finally, the cats' bladders were palpated and expressed every 6 h while sedated, and their bladders were not found to be overdistended at any time.

Neurogenic urinary retention in cats is due to impairment of the micturition 'reflex' and is described secondary to (1) upper motor neuron dysfunction due to lesions between the pons and the sacral spinal cord segments; (2) lower motor neuron dysfunction due to lesions in the sacral spinal cord segments, nerves of the cauda equina or peripheral nerves; and (3) feline dysautonomia.[5]

The coordinated and sustained contraction of the detrusor muscle and simultaneous relaxation of the urethral smooth and skeletal muscles represent the micturition 'reflex'.[7] The micturition 'reflex' requires complex integration of sensory and motor parasympathetic, sympathetic and somatic pathways extending from the sacral segments to the cerebral cortex.[7] The pontine micturition centres coordinate and control sphincter relaxation and detrusor contraction.[4] In particular, neurons located in the medial region of the dorsum of the pons, called the 'M-region', send their axons to the sacral spinal cord to excite the parasympathetic motor neurons and indirectly inhibit the somatic motor neurons in the Onuf's nucleus, facilitating bladder voiding.[8,9] Activation of neurons of the lateral region in the dorsum of the pons, called the 'L-region', facilitates urinary bladder filling, increasing the contraction of the external urethral sphincter via stimulation of the Onuf's nucleus.[8,9]

Experimental studies in cats and other mammals showed that many suprapontine structures are involved in micturition control, in particular the amygdala, basal nuclei, cerebellum, cerebral cortex, hypothalamus, insula, limbic system and periaqueductal grey matter (PAG).[10] During voiding, experimental and functional MRI studies in animals revealed activation of the anterior and lateral hypothalamic area, PAG, perigenual cingulate region and right anterior frontal gyrus.[10,11] Integration at the cortical level allows voluntary initiation or inhibition of micturition. Animals with cerebral cortical dysfunction may lose voluntary control of micturition.[7]

Postictal MRI studies have not been performed in the four cats described in this series. However, it is unlikely that the urinary retention following severe cluster seizures has been caused by a lesion affecting the brain stem or the spinal cord, as there was no evidence of involvement of these structures on repeated neurological examination. In all cats manual bladder expression was performed every 8 h until recovery of normal micturition. One cat was treated with phenoxybenzamine to reduce an initially supposed increase in internal urethral sphincter tone, to assist bladder expression. In all cats normal micturition and toileting behaviour recovered no later than 4 weeks after discharge. No further episodes of severe cluster seizure activity and urinary retention were reported by the owners, with follow-up periods ranging from 6 months to 3 years.

All cats required a CRI of propofol in addition to phenobarbital, levetiracetam and diazepam to control seizure activity. None of these medications have been described to cause urinary retention in cats.[12,13] In humans there are no descriptions of micturition disorder after phenobarbital, propofol and levetiracetam administration. Urinary retention has been described with other drugs, as a possible complication of long-term diazepam abuse and following continuous midazolam infusion in the treatment of uncontrollable neonatal seizures.[14,15] Therefore, it's unlikely that urine retention could be due to the antiepileptic treatment.

The urinary retention in our cat population was therefore regarded as a consequence of the cluster seizure activity. However, to the best of our knowledge, neurogenic urinary retention secondary to severe cluster seizures has not previously been reported in cats or dogs.

In humans, acute urinary retention due to structural disorders of the frontal lobe, paraventricular white matter, internal capsule and basal nuclei is well documented.[16] Furthermore, urinary retention has been reported as a transient postictal abnormality following epileptic seizure activity in humans.[17,18]

Postictal state (PS) is defined as the abnormal condition occurring between the end of an epileptic seizure and return to baseline condition.[19] The exact duration of the PS is difficult to define. Normally it lasts hours to a few days; however, PS can resolve over months to years.[19]

The mechanisms of the PS are poorly understood and likely multifactorial. They can be divided into electrophysiological mechanisms, cerebral blood flow changes, neurotransmitter system changes and receptor changes.[20]

In the human case series reporting urinary retention following epileptic seizures, the micturition disorder lasted up to 48 h.[17] It was hypothesised that a transient alteration of cortical activity on suprapontine micturition-associated structures could possibly result in postictal urinary retention. The transient alteration was suspected to be the consequence of seizure activity in the areas of the epileptic foci or areas adjacent to it.[17] Another study assessing peri-ictal urinary dysfunction in patients with epilepsy reported transient urinary retention exclusively in the postictal phase in 8.7% of the study population.[18] We suggest that a similar aetiopathogenesis may explain the urinary retention observed in our cats.

The far longer duration of urinary retention in our cat population compared with the human case series might be owing to the fact that the owners were instructed to

express the urinary bladder every 8 h, until the cats showed a normal eliminatory behaviour. This means that the urinary retention may have resolved earlier than 4 weeks. The passive voiding delayed the beginning of the spontaneous micturition, and may have resulted in us overestimating the duration of the urinary retention.

Another possibility is the occurrence of a long-lasting PS, characterised only by urinary retention, as described in humans.[19]

This previously unreported postictal abnormality in cats has a favourable prognosis if recognised and managed appropriately.

We speculate that this postictal abnormality may be unreported because it is uncommon, as per human literature, and potentially associated with severe cluster seizures only. This unreported postictal abnormality should be differentiated from a urinary tract disorder.

Conclusions

We report four cats with postictal transient neurogenic urinary retention following severe cluster seizures. All cats recovered normal urinary function and toileting behaviour within 4 weeks of the last cluster of seizures. We recommend monitoring of micturition in cats with severe cluster seizures and informing their owners that urinary retention may occur. Even if transient, it is necessary to diagnose and treat neurogenic urinary retention promptly to avoid secondary urinary tract infections and detrusor muscle atony.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding The authors received no financial support for the research, authorship and/or publication of this article.

References

1 Schmied O, Scharf G, Hilbe M, et al. **Magnetic resonance imaging of feline hippocampal necrosis**. *Vet Radiol Ultrasound* 2008; 49: 343–349.
2 Wahle AM, Brühschwein A, Matiasek K, et al. **Clinical characterization of epilepsy of unknown cause in cats**. *J Vet Intern Med* 2014; 28: 182–188.
3 Landsberg G, Hunthausen W and Ackerman L. **Feline housesoiling**. In: Landsberg G, Hunthausen W and Ackerman L (eds). Behavior problems of the dog and cat. 3rd ed. St Louis, MO: Saunders, 2013, pp 281–295.
4 Coates JR. **Tail, anal and bladder dysfunction**. In: Platt SR and Olby NJ (eds). BSAVA manual of canine and feline neurology. 4th ed. Gloucester: British Small Animal Veterinary Association, 2013, pp 381–387.
5 Olby NJ. **Neurogenic micturition disorders**. In: August JR (ed). Consultations in feline internal medicine. 5th ed. St Louis, MO: Saunders, 2006, pp 481–490.
6 Hostutler RA, Chew DJ and DiBartola SP. **Recent concepts in feline lower urinary tract disease**. *Vet Clin Small Anim* 2005; 35: 147–170.
7 Lorenz MD, Coates JR and Kent M. **Disorders of micturition**. In: Lorenz MD, Coates JR and Kent M (eds). Handbook of veterinary neurology. 5th ed. St Louis, MO: Saunders, 2011, pp 58–74.
8 Dewey CW. **Neurology and neuropharmacology of normal and abnormal urination**. In: Dewey CW (ed). A practical guide to canine and feline neurology. 2nd ed. Ames, IA: Wiley-Blackwell, 2008, pp 419–426.
9 Fowler CJ. **Neurological disorders of micturition and their treatment**. *Brain* 1999; 122: 1213–1231.
10 Griffiths DJ and Fowler CJ. **The micturition switch and its forebrain influences**. *Acta Physiol* 2013; 207: 93–109.
11 De Groat WC. **Central neural control of the lower urinary tract**. *Ciba Found Symp* 1990; 151: 27–44.
12 Bailey KS and Dewey CW. **The seizuring cat. Diagnostic work-up and therapy**. *J Feline Med Surg* 2009; 11: 385–394.
13 Finnerty KE, Barnes Heller HL, Mercier MN, et al. **Evaluation of therapeutic phenobarbital concentration and application of a classification system for seizures in cats: 30 cases (2004–2013)**. *J Am Vet Med Assoc* 2014; 244: 195–199.
14 Maany I, Greenfield H, Dhopesh V, et al. **Urinary retention as a possible complication of long-term diazepam abuse**. *Am J Psychiatry* 1991; 148: 685.
15 Hu KC, Chiu NC, Ho CS, et al. **Continuous midazolam infusion in the treatment of uncontrollable neonatal seizures**. *Acta Paediatr Taiwan* 2003; 44: 279–281.
16 Sakakibara R, Hattori T, Yasuda K, et al. **Micturitional disturbance after acute hemispheric stroke: analysis of the lesion site by CT and MRI**. *J Neurol Sci* 1996; 137: 47–56.
17 Vander T and Ifergane G. **Transient postictal urinary retention: presentation of three cases**. *Eur J Neurol* 2004; 11: 207–208.
18 Motamedi M, Nikoobakht MR, Aloosh M, et al. **Peri-ictal urinary disfunction in patients with epilepsy. A cross-sectional study**. *Urol J* 2011; 8: 222–226.
19 Fisher RS and Engel JJ, Jr. **Definition of the postictal state: When does it start and end?** *Epilepsy Behav* 2010; 19: 100–104.
20 Fisher RS and Schachter SC. **The postictal state: a neglected entity in the management of epilepsy**. *Epilepsy Behav* 2000; 1: 52–59.