Case Series

jfms Journal of Feline Medicine and Surgery

Feline ischaemic myelopathy with a predilection for the cranial cervical spinal cord in older cats

Journal of Feline Medicine and Surgery
2014, Vol. 16(12) 1001–1006

DOI: 10.1177/1098612X14522050
jfms.com

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Abstract

All previous studies on feline ischaemic myelopathy (IM) have reported an acute onset of a single event with no recurrence of clinical signs. This study aimed to evaluate clinical and long-term follow-up data in cats presumptively diagnosed with cervical IM in the territory of the ventral spinal artery (VSA). Eight cats (four females and four males) were included with a mean age of 14 years and 2 months. Neurological status at the time of presentation ranged from ambulatory tetraparesis to tetraplegia with nociception present. Six cats had marked cervical ventroflexion. All eight cats were diagnosed with one or more concurrent medical conditions, including chronic kidney disease (n = 2), hypertrophic cardiomyopathy (n = 2) and hypertension (n = 6). Median time to ambulation was 5.7 days (range 2–14 days). Long-term follow-up ranged from 7 months to 3 years and 3 months (median 1 year and 2 months). Five cats had no reported recurrence of clinical signs and 3/8 had a chronic relapsing disease course. One cat had an acute recurrence of clinical signs 4 months after the first event and was euthanased. Two cats had acute onsets of suspected intracranial infarctions, one of which had further suspected intracranial infarcts every 3 months and was euthanased after one of these. This study highlights the importance of performing ancillary diagnostic tests in older cats presenting with IM, particularly when VSA embolisation is suspected.

Accepted: 7 January 2014

Ischaemic myelopathy (IM) is a consequence of spinal cord vasculature occlusion and resultant ischaemic necrosis of the territory supplied.[1] IM has characteristic clinical and magnetic resonance imaging (MRI) features, yet histopathology is required for a definitive diagnosis.[2–4] Fibrocartilaginous embolic myelopathy (FCEM) is the most common cause of IM in dogs and cats,[3,5] although other causes include embolisation of thrombi, parasitic or septic emboli, vasculopathy and hypercoagulable states.[4,6] A retrospective study on histologically confirmed feline spinal cord diseases identified 11 cases of thrombosis or vasculopathy of unknown cause.[7] The aim of this study is to report a novel subtype of feline cervical IM resulting from ischaemia of the ventral spinal artery (VSA) with defining clinical and MRI features. The clinical outcome of three cats included in this study has been reported elsewhere.[5]

Materials and methods

The medical databases of two UK veterinary referral hospitals were examined to identify cats presumptively diagnosed with IM. Inclusion criteria comprised a peracute (<6 h) to acute (7–24 h) onset of myelopathy with neurolocalisation to the C1–T2 spinal cord segments, MRI of the cervical spine performed (consisting of T2-weighted [T2W] sagittal and transverse images) with findings compatible with an IM in the vascular territory of the VSA, comprehensive medical records, and a minimum of 6 months' follow-up information. MRI findings compatible with IM in the vascular territory of the VSA included an intramedullary, ventrally located, symmetrical, well-demarcated, elliptical, hyperintense lesion on T2W and fluid-attenuated inversion recovery transverse images (Figure 1) with no contrast enhancement. Cases

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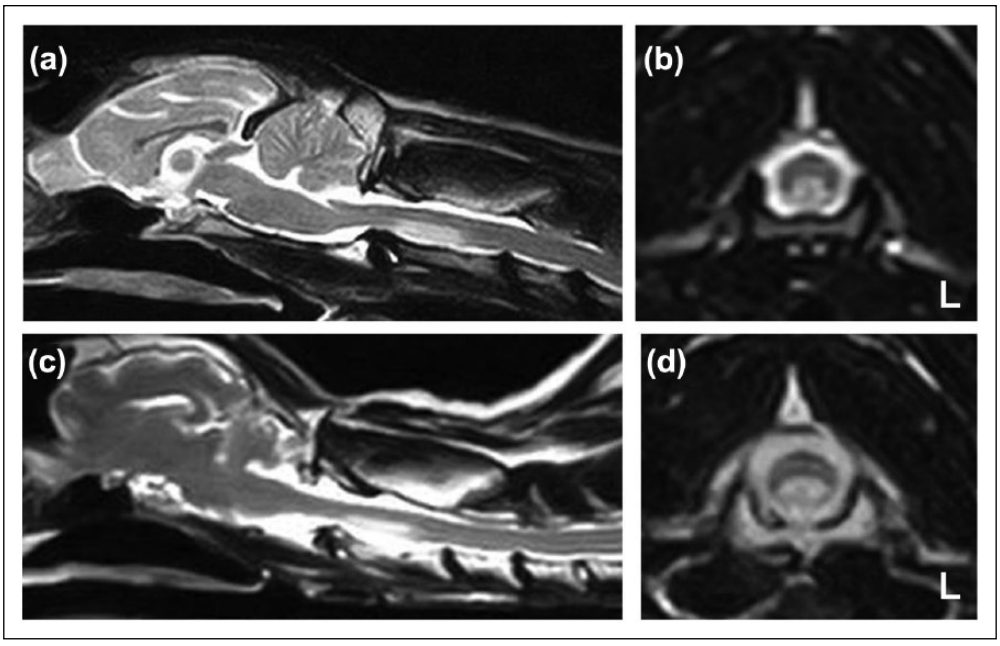

Figure 1 T2-weighted sagittal and transverse images of the cervical spinal cord of cats 1 (a,b) and 2 (c,d). A ventral hyperintense lesion is seen at the level of C2 on the sagittal images (a,c). An analogous ventral hyperintense elliptical lesion is seen in the transverse images (b,d) corresponding to the territory of the ventral spinal artery at C2

that had a history of trauma, or that had MRI evidence of intervertebral disc disease ventral to the intramedullary spinal cord lesion (loss of annulus fibrosus integrity or decreased nucleus pulposus volume) were excluded. Magnetic resonance (MR) images were acquired using a 0.4 Tesla MRI scanner (Hitachi Aperto) or 1.5 Tesla MRI scanner (Sigma echospeed superconducting magnet; General Electric Medical Systems). All MR images were examined by board-certified radiologists.

Information recovered from the medical records included age at onset, sex, breed, clinical signs, neurolocalisation, presence or absence of cervical ventroflexion, results of any ancillary diagnostic tests performed, concurrent medical conditions and cerebrospinal fluid (CSF) analysis results. Cats were allocated a neurological grade based upon neurological examination findings at the time of presentation of 1 (normal), 2 (ambulatory tetraparesis), 3 (non-ambulatory tetraparesis) and 4 (tetraplegic with nociception present). Long-term follow-up information was acquired from the patients' records, and from either the owners or referring veterinary surgeons via a telephone questionnaire. A recurrence of thromboembolic disease (either an IM or cerebrovascular accident) was suspected based on a peracute/acute onset of non-progressive clinical signs with rapid improvement.

Results

Eight cats were included (Table 1) with a mean age at time of presentation of 14 years and 2 months (median 14 years; range 12 years 11 months to 16 years). Four cats were male neutered and four were female neutered. Breeds comprised the domestic shorthair (n = 4), domestic longhair (n = 2) and Persian (n = 2).

Clinical and MRI findings

Neurological grade at time of presentation ranged from 2 (ambulatory tetraparesis) to 4 (tetraplegic with nociception present) (Table 1), with six cats (75%) scored as 3 (non-ambulatory tetraparesis). Six cats displayed marked cervical ventroflexion.

In all eight cats, MRI of the cervical spinal cord revealed the aforementioned lesion at the level of the C2 or C3 vertebra (Figure 1). Clinical and MRI neurolocalisations correlated in all but one case (Table 1; cat 2).

Ancillary diagnostic tests performed included haematology (n = 7), serum biochemistry (n = 8), serum total T4 concentration (n = 6), serial Doppler blood pressure measurements (n = 8), urinalysis (n = 4), thoracic radiographs (n = 8), abdominal ultrasound (n = 7), cardiac ultrasound (n = 3) and CSF analysis (n = 8). Six cats were diagnosed as hypertensive (systolic blood pressure >180 mmHG),[8] two with hypertrophic cardiomyopathy (HCM) and two with chronic kidney disease (CKD). CSF analysis detected increased total protein concentrations (>0.3 g/l) in three cats, one of which also had an increased nucleated cell count (Table 1; cat 1).

Outcome

All cats received supportive care (eg, hand-feeding and intravenous crystalloid fluid administration for

Table 1 Signalment and outcome of eight cats with C2 or C3 ischaemic myelopathy detected on magnetic resonance imaging (MRI)

Cat	Age	Sex	Breed	Neurological grade	Neuro localisation	Cervical segment affected on MRI	Cervical ventroflexion	CSF	Concurrent medical conditions	Time to ambulation (days)	Outcome (months after presentation)	Current medications
1	14 y	MN	DLH	3	C1–C5	C2	Yes	TP 1.09 g/l (N <0.3) NCC 13/µl (N <5) Eosinophilic pleocytosis (60%)	Hypertension CKD	5	NQol (12)	Clopidogrel (18.75 mg q24h)
2	13 y	MN	Persian	4	C1–T2	C2	Yes	WNL	Hypertension	7	NQoL (18)	Clopidogrel (18.75 mg q24h)
3	15 y 7 mo	FN	DSH	2	C1–C5	C2	No	WNL	Hypertension	N/A	NQoL (17)	Amlodipine (1.25 mg q24h)
4	15 y	FN	DSH	3	C1–C5	C2	Yes	Contaminated	HCM and mitral valve degeneration	5	NQoL (7)	None
5	12 y 11 mo	FN	DSH	3	C1–C5	C3	Yes	WNL	Hypertension HCM	4	LTF after 39 mo	None at time of discharge
6	13 y	MN	DLH	3	C1–C5	C3	Yes	TP 0.38g/l	Hypertension	14	NQoL (18) then further suspected infarcts every 3 months. Euthanased (30) after one of these	N/A
7	16 y	MN	DSH	3	C1–C5	C3	No	WNL	Hypertension	3	NQoL (10)	Amlodipine (0.125 mg q24h) Benazepril (2.5 mg q24h)
8	14 y 6 mo	FN	Persian	3	C1–C5	C3	Yes	TP 0.85 g/l	CKD	2	NQoL (2); euthanased (4) after further suspected infarct	N/A

CSF = cerebrospinal fluid; y = years; mo = months; MN = male neutered; FN = female neutered; DLH = domestic longhair; DSH = domestic shorthair; TP = total protein; NCC = nucleated cell count; WNL = within normal limits; CKD = chronic kidney disease; HCM = hypertrophic cardiomyopathy; NQoL = normal quality of life; LTF = lost to follow-up; N/A = not applicable

rehydration and maintenance therapy until eating normally) and physiotherapy (performed by qualified veterinary nurses and/or physiotherapists consisting of kneading massage, passive range of movement exercises, and strengthening and functional coordination exercises) during hospitalisation, although this treatment varied between cases and hospitals. For the seven cats that were non-ambulatory upon presentation, the mean time to ambulatory was 5.7 days (median 5 days; range 2–14 days). Two cats were prescribed prophylactic anti-platelet clopidogrel (18.75 mg orally once daily) therapy on discharge, and two cats were treated for hypertension with amlodipine (1.25 mg orally once daily). One of these was additionally prescribed benazepril (2.5 mg orally once daily) owing to continued hypertension at re-examination 5 days later.

Long-term follow-up data were available for all eight cats with a mean time to follow-up of 1 year and 6 months (median 1 year and 2 months; range 4 months to 3 years and 3 months). All cats returned to normal or nearly normal neurological function over the proceeding few months after discharge, with residual deficits reported to be mild ataxia (Table 1; cats 1, 3, 4) and tetraparesis (case 7). Five cats had no reported recurrence of clinical signs, with a median time to follow-up of 1 year and 6 months (range 7 months to 3 years and 3 months). One of these (cat 5) was lost to follow-up after 3 years and 3 months.

Three cats had a chronic relapsing disease course. Cat 6 returned to a normal quality of life with no neurological deficits 2 weeks after onset of the first event. Eighteen months later the cat was afflicted with an acute onset of non-progressive vestibulocerebellar signs, which were never investigated by a neurologist, and made a full recovery within 3 days. Recurrence of vestibulocerebellar signs followed by a similarly rapid recovery period was reported to occur approximately every 3 months. Thirty months after the first event the cat was euthanased at the owner's request owing to a severe peracute onset of vestibulocerebellar signs. Cat 7 had an acute onset of right-sided forebrain signs 32 days after the first event. The cat had been prescribed amlodipine after the first event, and adjunctive benazepril treatment was prescribed after detection of continued hypertension on investigation of the second event. The cat was ambulatory 2 days after this second event with return to normal quality of life 25 days later. Cat 8 returned to normal neurological function after the first event and was subsequently prescribed antibiotics for a chronic urinary tract infection. Four months after the first event it suffered an acute onset of tetraplegia and was euthanased on presentation at the owner's request without further investigation or treatment.

Discussion

We report eight cases of IM in older cats with characteristic findings of an acute onset of C1–C5 myelopathy, low head carriage in the majority of cases, the presence of concurrent medical conditions, and the potential for a chronic and relapsing disease course. This presentation appears distinct from FCEM, which usually causes a single event in cats with no concurrent medical conditions, and has been reported in cats as young as 6 months of age.[5]

All eight cats presented with an acute onset of non-progressive signs. Neurological severity ranged from ambulatory tetraparesis (grade 2) to tetraplegia (grade 4) consistent with previous IM reports.[5] Six out of eight cats exhibited marked ventroflexion of the neck. This has been reported in association with neuromuscular weakness and severe grey matter lesions of the brain or cervical spinal cord.[9–11] The cervical ventroflexion reported here was suspected to be due to the cervical grey matter involvement and is distinct from these other causes in that it presented acutely. We hypothesise that this posture is most likely observed owing to paresis of the cervical dorsal epaxial muscles. The strength of these muscles is likely more important than in dogs in maintaining an erect position of the head owing to the anatomical absence of the nuchal ligament in cats.

The symmetry of clinical signs was atypical from the majority of histologically confirmed FCEM cases.[2,4,12–14] Increased CSF protein concentrations detected in three cats, and increased NCC detected in one cat, was in agreement with previous reports of feline IM cases.[12,14] CSF pleocytosis in all previous feline cases was neutrophilic; however, in some canine cases this has been reported as mixed.[5,15] Conversely, eosinophilic pleocytosis has never been reported in IM, although it has been described in canine cerebrocortical infarction.[16] Following discharge, all cats exhibited a gradual return to normal neurological function, albeit some with persistent mild neurological deficits. Two recent studies similarly reported a preponderantly favourable prognosis for feline IM cases.[5,17] The recurrence of original neurological signs in one cat, and subsequent occurrence of suspected intracranial central nervous system infarcts in two other cats has, however, never been reported in feline IM cases.

Feline IM may affect any spinal cord segment.[5,13] MRI findings correlated with clinical neurolocalisation in 7/8 cats. Neurolocalisation to C6–T2 was made in one cat based on reduced thoracic limb flexor withdrawal reflexes, yet MRI revealed an intramedullary lesion at C2. Withdrawal reflex testing has, however, been reported as an unreliable neurolocalisation method in dogs and this is likely also the case in cats.[18] All cats displayed a characteristic elliptical lesion on MRI affecting the ventral spinal cord over the C2 or C3 vertebral bodies confined to the vascular territory of the VSA. One feline IM retrospective study reported analogous lesions in all six cases localising to the C1–C5 segments.[5] Four of

these were diagnosed with concurrent medical conditions and one had a history of trauma.[5] Three of these cases met our inclusion criteria and were thus included in our study (Table 1; cats 3, 5 and 6). The feline VSA is narrowest at C2, which provides a conceivable explanation for this apparent predisposition to embolisation at C2.[19] Anatomical variation of the VSA between cats provides a plausible reason for MRI lesion detection at the level of the C3 vertebral body in some cases. In humans, the pattern of cervical radicular arteries in the cervical region has led to the suggestion that a minor watershed zone exists at C4.[20] A watershed zone refers to an area that receives dual blood supply from two or more arteries. These zones are particularly susceptible to ischaemia as they are supplied by the most distal branches of their arteries and hence the least likely to receive sufficient blood flow. Therefore, a similar phenomenon cannot be excluded in cats, although this has not been investigated.

In cats, potential risk factors predisposing to thrombosis or embolisation include CKD, hypertension, cardiomyopathy and hyperthyroidism.[4,5] Concurrent medical conditions, including CKD, hypertension HCM, were diagnosed in all of our cats. A study investigating canine cerebrovascular accidents (CVA) identified concurrent medical conditions in over 50% of cases. Furthermore, these dogs had a significantly increased risk of developing subsequent infarcts.[21] In humans, vertebral strain has been reported in conjunction with cervical anterior spinal artery thrombosis and myelomalacia.[22] Feline IM may likewise be associated with triggering movements or trauma.[5] Cerebral amyloid angiopathy, a common cause of CVA in humans, has been reported in geriatric cats.[23,24] Detection of congophilic β-amyloid protein at post-mortem examination would be interesting, but has not been investigated in our study owing to the excellent improvement in the majority of cases and to the inability to obtain permission from the owners to perform post-mortem examination in the two cats euthanased.

Thromboembolic disease resulting in IM is suspected, but cannot be confirmed. The high incidence of concurrent medical conditions in older cats suggests a pathogenesis that differs from feline FCEM. Repeat MRI was not performed in those cats that had recurrence of neurological signs on ethical grounds, yet the presence of concurrent medical conditions predisposing to thromboembolism is supported by the occurrence of recurrent thromboembolic events alongside the acute onset of non-progressive clinical signs with rapid improvement, as shown in cats 6 and 7. Further limitations of this multicentre retrospective study were the disparity of management protocols (eg, varying management of hypertension and concurrent disease) and small number of cases. Lifelong prophylactic antiplatelet therapy was prescribed to two cats, yet no controlled veterinary studies have evaluated this prophylaxis.[25] Future studies may provide additional information regarding long-term prognostic factors in feline IM cases with concurrent medical conditions.

Conclusions

We present eight cases of feline cervical IM emphasising the apparent predisposition of the VSA at C2 or C3 to embolic occlusion. All cats were older than 12 years with concurrent medical conditions. Novel features included an acute onset of cervical ventroflexion and a chronic relapsing course in 3/8 cases. Initial prognosis for return to function appears favourable regardless of neurological grade, yet concurrent medical conditions may predispose to secondary ischaemic events. MRI had a characteristic appearance distinct from previous reports of FCEM and IM. Our findings highlight the importance of ancillary diagnostic testing in older cats presenting with clinical and MRI signs suggestive of IM, particularly when involvement of the VSA is suspected.[5]

Conflict of interest The authors do not have any potential conflicts of interest to declare.

Funding The authors received no specific grant from any funding agency in the public, commercial or not-for-profit sectors for the preparation of this case series.

References

1 Cummings JF, De Lahunta A and Summers BA. **Degenerative diseases of the central nervous system**. In: Cummings JF, De Lahunta A and Summers BA (eds). Veterinary neuropathology. St Louis, MO: Mosby, 1995, pp 208–350.
2 Coradini M, Johnstone I, Filippich I, et al. **Suspected fibrocartilaginous embolism in a cat**. *Aus Vet J* 2005; 83: 550–551.
3 Cauzinille L and JN Kornegay JN. **Fibrocartilaginous embolism of the spinal cord in dogs: review of 36 histologically confirmed cases and retrospective study of 26 suspected cases**. *J Vet Intern Med* 1996; 10: 241–245.
4 Turner PV, Percy DH and Allyson K. **Fibrocartilaginous embolic myelopathy in a cat**. *Can Vet J* 1995; 36: 712–713.
5 Theobald A, Volk H, Dennis R, et al. **Clinical outcome in 19 cats with clinical and magnetic resonance imaging diagnosis of ischaemic myelopathy (2000–2011).** *J Feline Med Surg* 2012; 15: 132–141.
6 Dyce J and Houlton JF. **Fibrocartilaginous embolism in the dog**. *J Small Anim Pract* 1993; 34: 332–336.
7 Marioni-Henry K, Vite C, Newton A, et al. **Prevalence of diseases of the spinal cord of cats**. *J Vet Intern Med* 2004; 18: 851–858.
8 Brown S, Atkins C, Bagley R, et al. **Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats**. *J Vet Intern Med* 2007; 21: 542–558.
9 Dickinson PJ and LeCouteur RA. **Feline neuromuscular disorders**. *Vet Clin North Am Small Anim Pract* 2004; 34: 1307–1359.

10 Vidal E, Montoliu P, Añor S, et al. **A novel spongiform degeneration of the grey matter in the brain of a kitten**. *J Comp Path* 2004; 131: 98–103.
11 Palus V, Penderis J, Jakovljevic S, et al. **Thiamine deficiency in a cat: resolution of MRI abnormalities following thiamine supplementation**. *J Feline Med Surg* 2010; 12: 807–810.
12 Abramson CJ, Platt SR and Stedman NL. **Tetraparesis in a cat with fibrocartilaginous emboli**. *J Am Anim Hosp Assoc* 2002; 38: 153–156.
13 MacKay AD, Rusbridge C, Sparkes AH, et al. **MRI characteristics of suspected acute spinal cord infarction in two cats, and a review of the literature**. *J Feline Med Surg* 2005; 7: 101–107.
14 Mikszewski JS, Van Winkle TJ and Troxel MT. **Fibrocartilaginous embolic myelopathy in five cats**. *J Am Anim Hosp Assoc* 2006; 42: 226–233.
15 De Risio L, Adams V, Dennis R, et al. **Magnetic resonance imaging findings and clinical associations in 52 dogs with suspected ischemic myelopathy**. *J Vet Intern Med* 2007; 21: 1290–1298.
16 Vandevelde M and Spano JS. **Cerebrospinal fluid cytology in canine neurologic disease**. *Am J Vet Res* 1977; 38: 1827–1832.
17 Nakamoto Y, Ozawa T, Mashita T, et al. **Clinical outcomes of suspected ischaemic myelopathy in cats**. *J Vet Med Sci* 2010; 72: 1657–1660.
18 Forterre F, Konar M, Tomek A, et al. **Accuracy of the withdrawal reflex for localization of the site of cervical disc herniation in dogs: 35 cases (2004–2007)**. *J Am Vet Med Assoc* 2008; 232: 559–563.
19 Bradshaw P. **Arteries of the spinal cord in the cat**. *J Neurol Neurosurg Psychiat* 1958; 21: 284–289.
20 Cheshire WP, Santos CC, Massey EW, et al. **Spinal cord infarction: etiology and outcome**. *Neurology* 1996; 47: 321–330.
21 Garosi L, McConnell J, Platt S, et al. **Results of diagnostic investigations and long-term outcome of 33 dogs with brain infarction (2000–2004)**. *J Vet Intern Med* 2005; 19: 725–731.
22 Grinker R and Guy C. **Sprain of cervical spine causing thrombosis of anterior spinal artery**. *J Am Med Assoc* 1927; 88: 1140–1142.
23 Vonsattel J, Myers R, Hedley-White E, et al. **Cerebral amyloid angiopathy without and with cerebral hemorrhages: a comparative histological study**. *Annals Neurol* 1991; 30: 637–649.
24 Nakamura S, Nakayama H and Kiatipattanasakul W. **Senile plaques in very aged cats**. *Acta Neuropathol* 1996; 91: 437–439.
25 Garosi LS. **Cerebrovascular disease in dogs and cats**. *Vet Clin North Am Small Anim Pract* 2010; 40: 65–79.