PAPER

Clinical presentation, diagnostic findings and outcome in dogs diagnosed with presumptive spinal-only meningoencephalomyelitis of unknown origin

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Objectives: To summarise clinical presentation, diagnostic findings and long-term outcome for dogs clinically diagnosed with meningoencephalomyelitis of unknown origin affecting the spinal cord alone.

Methods: Medical records were reviewed for dogs diagnosed with presumptive spinal-only meningoencephalomyelitis of unknown origin between 2006 and 2015.

Results: 21 dogs were included; the majority presented with an acute (43%) or chronic (52%) onset of neurological signs. Ambulatory paresis was the most common neurological presentation (67%). Neurological examination most commonly revealed a T3-L3 myelopathy, and spinal hyperaesthesia was a common finding (71%). A spinal cord lesion was visible in 90% of cases on magnetic resonance imaging. Eighteen lesions (86%) showed parenchymal contrast enhancement and 17 lesions (81%) showed contrast enhancement of overlying meninges. All dogs were treated with immunosuppressive doses of glucocorticosteroids, sometimes combined with cytosine arabinoside. At time of data capture, 10/21 dogs (48%) had died or been euthanased because of the condition. Overall median survival time was 669 days.

Clinical Significance: Meningoencephalomyelitis of unknown origin should be considered in the differential diagnosis of dogs presenting with a progressive myelopathy. Magnetic resonance imaging features can possibly help to distinguish presumptive meningoencephalomyelitis of unknown origin from other more common spinal diseases. Overall, long-term survival is guarded, approximately 50% of dogs will die or be euthanased despite appropriate therapy.

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INTRODUCTION

Pure myelitis (inflammation of spinal cord parenchyma) or meningomyelitis (inflammation of spinal cord parenchyma and surrounding meninges) are rare diseases in small animals but occur most often in combination with inflammatory brain disease (Tipold & Stein 2010). Viruses [canine distemper virus (CDV), feline coronavirus], bacteria (*Staphylococcus* species, *Streptococcus* species, *Pasteurella*, coliforms, *Actinomyces*, *Nocardia* species), fungi (*Cryptococcus*, *Coccidioides* species, *Blastomyces*, *Histoplasma*), rickettsiae (*Ehrlichia*, *Rickettsia*, Rocky Mountain spotted fever), protozoa (*Toxoplasma gondii*, *Neospora caninum*), parasites (*Dirofilaria immitis*, *Cuterebra*, *Angiostrongylus vasorum*) and algae (*Prototheca wickerhamii*, Prototheca *zopfii*) are known causes for meningomyelitis in dogs and cats, with or without concurrent intracranial signs (Griffin *et al.* 2008, Parry

et al. 2009, Csebi *et al*. 2010, Dewey *et al*. 2016). Apart from infectious causes, non-infectious meningoencephalomyelitis including granulomatous meningoencephalomyelitis, pyogranulomatous meningoencephalomyelitis and steroid-responsive meningitis-arteritis (SRMA) are described (Meric 1988, Griffin *et al*. 2008, Parry *et al*. 2009, Dewey *et al*. 2016). Current terminology implies that dogs clinically diagnosed with non-infectious inflammatory myelitis without positive infectious disease testing, not classified as SRMA or eosinophilic meningomyelitis, and not histopathologically confirmed with alternative diagnoses are categorised as having meningoencephalomyelitis of unknown origin (MUO), equivalent to dogs diagnosed with meningoencephalitis of unknown origin. A clinical diagnosis of MUO is typically made by a combination of clinical presentation, MR imaging of involved part of the central nervous system (brain/spinal cord), and results of cerebrospinal fluid (CSF) analysis (Griffin *et al*. 2008).

Currently, only one study has focused specifically on the clinical presentation, diagnostic findings and outcome in dogs with meningomyelitis caused by a variety of underlying aetiologies (Griffin *et al*. 2008). Of 28 cases included, 15 dogs were diagnosed with MUO. Clinical signs were reflected by the affected spinal cord segments, and younger dogs, toy breeds, and hound breeds were suggested to be predisposed for meningomyelitis. Although results of myelography, CT, and CT-myelography have been reported, little is reported about magnetic resonance imaging (MRI) findings in dogs with MUO of the spinal cord. The aims of this study were therefore to describe the signalment, clinical presentation, diagnostic findings, including results of MRI and long-term survival in dogs diagnosed with presumptive MUO of the spinal cord without concurrent clinical signs of intracranial involvement.

MATERIALS AND METHODS

Case selection

The electronic medical database was searched between March 2006 and February 2015 for dogs diagnosed with "MUA," "MUO," "GME," "myelitis," "inflammatory spinal cord disease." Dogs were included based on the criteria used by Granger *et al*. (2010), if they had (1) complete medical records available, (2) a complete neurological examination performed leading to a spinal cord localisation, (3) inflammatory CSF analysis, (4) MRI of the spinal cord and if (5) long-term follow-up information were available through revision of medical records or through contacting the referring veterinarian by telephone. Dogs were excluded if (1) the clinical records or imaging studies were incomplete or not available for review, (2) dogs showed clinical or neurological signs of intracranial involvement at time of presentation, (3) they had a peracute onset of clinical signs that were not progressive after 12 to 24 hours, (4) they had signs of extradural or extradural/intramedullary spinal cord compression on MRI and if (5) they had positive infectious disease titres or if clinical presentation, CSF analysis or necropsy findings were suggestive of SRMA or eosinophilic meningoencephalomyelitis (>10% eosinophils in CSF) (Dewey *et al*. 2016). Typical clinical presentation for SRMA was considered to be a dog less than 2 years of age of a typical breed (boxer, beagle, Bernese mountain dog, Nova Scotia duck tolling retriever, golden retriever, German shorthaired pointer) presenting with pyrexia and cervical hyperesthesia. CSF analysis in SRMA typically reveals a predominantly neutrophilic pleocytosis (Dewey *et al*. 2016). Dogs with histopathological confirmation of the disease [granulomatous meningo(encephalo)myelitis (GME) or necrotising meningo(encephalo)myelitis (NME) only needed to fulfil inclusion criteria (1) and (5). Information retrieved from the medical records included breed, gender, age at diagnosis, body weight, results of neurological examination including neuroanatomical localisation, duration of clinical signs prior to diagnosis, results of complete blood count (CBC) and biochemistry profile, results of CSF analysis including total nucleated cell count (TNCC), white blood cell differentiation and total protein (TP) concentration, treatment received and outcome. Duration of clinical signs prior to diagnosis (days) was classified as peracute (<2 days), acute (2 to 7 days) or chronic (>7 days). For dogs that had CSF analysis performed, site of collection (cisternal or lumbar), TNCC, TP and cytological differentiation were recorded. TNCC was considered normal if there were <5 cells/mm^3. Protein concentration was considered normal for a cisternal collection if <0·25 g/L and for a lumbar collection if <0·4 g/L.

Neurological assessment

The neurological status was classified from 0 to 5 according to the clinical examination (adapted from Scott 1997): grade 0=neurologically normal; grade 1=spinal hyperaesthesia without neurological deficits; grade 2=ataxia, ambulatory para- or tetraparesis; grade 3=non-ambulatory para- or tetraparesis; grade 4=para- or tetraplegia with or with- out bladder control, and intact deep pain sensation; grade 5=para- or tetraplegia, urine retention or overflow, and deep pain sensation loss.

Possible neuroanatomical localisations included C1 to C5, C6 to T2, T3 to L3 or L4 to S3 spinal cord segments. Dogs were diagnosed with a focal lesion if only one spinal cord segment was affected, and with a multifocal lesion if more than one spinal cord segment appeared to be affected on the neurological examination.

Magnetic resonance imaging

MRI was performed under general anaesthesia with a permanent 1.5-T magnet (Intera, Philips Medical Systems, Eindhoven, the Netherlands) and all images were reviewed by the corresponding author using Osirix Dicom viewer (Osirix Foundation, V.5.5.2 Geneva, Switzerland). Sequences varied, but included a minimum of T2-weighted (T2W) [repetition time (ms) (TR)/echo time (ms) (TE), 3000/120] and T1-weighted (T1W) (TR/TE, 400/8) images of the affected spinal cord region in a sagittal and transverse plane. The T1W images were acquired before and after intravenous (IV) administration of paramagnetic contrast medium with a dose of 0·1 mg/kg gadoterate meglumine (Dotarem, Guerbet). If MR images of the brain were available, they were reviewed concurrently. Variables recorded were lesion

intensity on T2W and T1W images, lesion localisation and distribution, lesion length and parenchymal and/or meningeal contrast enhancement. Lesion length was measured using Osirix Dicom viewer, and performed on sagittal T2W images for dogs that had focal lesions. Lesion length was measured twice, and the mean value reported. To compensate for differences in body size, values were corrected with respect to the length of vertebral body of C6 (for cervical lesions) or L2 (for thoracolumbar lesions). Vertebral body length was measured on T1W sagittal images.

Treatment and follow-up

For all dogs, the specific treatment protocol was recorded. During hospitalisation, all dogs underwent daily at least one general physical and complete neurological examination by a board-certified neurologist or neurology resident. The results of the neurological examination as well as response to treatment (improvement, deterioration or static) were systematically recorded on the kennel sheets. Follow-up information during hospitalisation was collected from the medical records, and later through medical records of re-examination visits or telephone contact with the referring veterinarian. A successful outcome was defined as the dog being ambulatory, with faecal and urinary continence and, according to the owners, without overt spinal hyperaesthesia. An unsuccessful outcome was defined as (1) deterioration in neurological status by one or more grades after diagnosis and treatment or (2) if the dog was not independently ambulatory, possibly with previously non-existing or worsening faecal and/or urinary incontinence, or was experiencing spinal hyperaesthesia as defined by the owner.

Statistical analysis

Data analysis was performed with the aid of a standard statistical software package (Prism, Graphpad Software Inc). Numeric variables were expressed as median and interquartile ranges (IQR). Values of $P<0{\cdot}05$ were considered significant. Survival analysis was performed using both a Log-rank (Mantel-Cox) and Gehan-Breslow-Wilcoxin test, resulting in median survival time (MST) calculation and a Kaplan-Meier survival curve.

Survival was defined as time from diagnosis to death or euthanasia, including whether this happened because of disease progression or due to unrelated causes, or time from diagnosis to last follow-up for dogs that were alive at time of data capture. Dogs that died because of unrelated causes and dogs that were still alive at time of data capture were censored for survival analysis.

RESULTS

Signalment

Twenty-one dogs were included in the study. Represented breeds included French bulldog (n=2), Jack Russell terrier (n=2), Lhasa apso (n=2) and one each of akita, bearded collie, boxer, bull mastiff, Chihuahua, cross breed, English springer spaniel, giant schnauzer, Labrador retriever, Maltese terrier, Rhodesian ridgeback, rottweiler, shih-tzu, West Highland white terrier and Yorkshire terrier. Overall, median age at presentation was 56 months (10 to 128 months). Thirteen dogs (62%) were male and eight (38%) were female. Compared to the general hospital population between March 2006 and February 2015, there was no difference in sex distribution in the group of dogs with MUO (Fisher's exact test; $P=0{\cdot}075$). Median duration of clinical signs prior to diagnosis was eight days (ranging from 1 to 90 days). One dog (5%) presented with peracute, nine dogs (43%) with acute and eleven dogs (52%) with a chronic onset of neurological signs.

Neurological examination

Thirteen (62%) and eight (38%) dogs were diagnosed with a focal and multifocal spinal lesion on neurological examination, respectively. For dogs with focal spinal lesions (n=13), three were diagnosed with a lesion affecting the C1 to C5 spinal cord segments, two with a lesion affecting the C6 to T2 spinal cord segments, six with a lesion affecting the T3 to L3 spinal cord segments and two with a lesion affecting the L4 to S3 spinal cord segments. At time of diagnosis, no dogs presented as grade 0; 2 dogs (10%) were grade 1; 14 (67%) grade 2 and 5 (24%) grade 3. No dogs were paraplegic or tetraplegic at presentation. Pain on direct spinal palpation was present in 15 (71%) dogs. Urinary retention was observed in two dogs (10%), and a combination of urinary and faecal incontinence was noticed in two dogs (10%). One dog (5%) developed seizures 669 days after diagnosis of MUO. Clinical findings of the 21 included dogs are summarised in Table 1.

Diagnostic findings

As required by the inclusion criteria, CSF collection revealed pleocytosis in all cases. Overall, median TNCC was 209 cells/mm^3 (ranging from 6 to 6000). TP measurement was performed in all but three CSF samples, and was above reference values in 17/18 dogs (94%). The median TP concentration was 1·67 g/L (ranging from 0·21 to 16·3 g/L). CBC and serum biochemistry results were available in 16 dogs (76%). Leucocytosis was only present in two dogs (10%) and lymphopenia was present in six dogs (29%). Infectious disease testing based on serology and/or polymerase chain reaction on CSF for CDV, *T. gondii*, and *N. caninum* was not performed in two (10%) dogs and was negative in the remaining 19 (90%) dogs. In the two dogs lacking infectious disease testing, full necropsy was performed, revealing GME.

Magnetic resonance imaging

MRI of the spinal cord was available in all cases, revealing a focal lesion in 15 dogs (71%), a multifocal lesion in four (19%) and no lesion was visible on sagittal T2W or T1W images in two (10%). Lesion length was measured in the focal cases only. Median lesion/vertebral body ratio was 4·8 (ranging from 0·6 to 10·9). All visible lesions were ill-defined, intramedullary, hyperintense on T2W images and isointense on T1W images (Figs 1 and 2). Lesions showed parenchymal contrast enhancement in 18 dogs (86%), and contrast enhancement of overlying meninges in 17 (81%). In the two cases in which no lesion was visible on sagittal T2W and T1W images, there was also no observable parenchymal contrast, but one dog only showed meningeal

Table 1. Clinical Details of the 21 Dogs Diagnosed with Spinal MUO

Case	Breed	Gender	Age (months) at presentation	Clinical presentation	Neuro-anatomical localisation	Spinal hyper-aesthesia	CSF TNCC (cells/μL)	MRI lesion	Initial treatment	Cytosine arabinoside dose (mg/m²), SC or CRI	Initial response to treatment	Long-term follow-up and treatment	Death or euthanaseda because of MUO	Overall ST (days)	Post-mortem examination findings
1	Akita	FE	36	Non-ambulatory paraparesis	Multifocal	Yes	1740	Focal	2 mg/kg/day prednisolone	50 mg/m² sc	Improvement	Euthanased because of acute deterioration after discontinuation of prednisolone treatment	Yes	380	NP
2	Rottweiler	ME	123	Ataxia	T3 to L3	No	209	Focal	2 mg/kg/day prednisolone	50 mg/m² sc	Deterioration	Euthanased because of disease progression	Yes	20	NP
3	Bull mastiff	ME	42	Ambulatory paraparesis	T3 to L3	Yes	6	No lesion visible	2 mg/kg/day prednisolone	No cytosine arabinoside	Deterioration	Euthanased because of disease progression	Yes	6	NP
4	Labrador	MN	105	Ambulatory paraparesis	L4 to S3	Yes	123	Focal	0·3 mg/kg/day dexa-methasone	50 mg/m² sc	Improvement	Euthanased because of acute deterioration, was still receiving a dose of 1 mg/kg prednisolone every day	Yes	30	NP
5	Jack Russell terrier	MN	89	Ambulatory paraparesis	T3 to L3	No	200	Focal	2 mg/kg/day prednisolone	No cytosine arabinoside	Improvement	Normal dog, still receiving a dose of 0·2 mg/kg/day prednisolone	No	237	NA
6	Lhasa apso	FE	48	Ambulatory tetraparesis	C1 to C5	Yes	900	Focal	4 mg/kg/day prednisolone	50 mg/m² sc	Improvement	Euthanased because of acute deterioration, was still receiving a dose of 0·5 mg/kg prednisolone per day	Yes	171	GMEM
7	Shih tzu	MN	50	Ambulatory tetraparesis	C6 to T2	Yes	5	Focal	2 mg/kg/day prednisolone	50 mg/m² sc	Improvement	Normal dog, receiving a dose of 5 mg/kg/day cyclosporine	No	2250	NA
8	Giant schnauzer	ME	32	Non-ambulatory paraparesis	Multifocal	No	1345	Focal	2 mg/kg/day prednisolone	50 mg/m² sc	Improvement	Euthanased because of agression, was only receiving cytosine arabinoside every 5 weeks	No	752	NP
9	Yorkshire terrier	FN	36	Ambulatory tetraparesis	C1 to C5	Yes	7	Focal	2 mg/kg/day prednisolone	No cytosine arabinoside	Improvement	Euthanased because of acute deterioration, was still receiving a dose of 1 mg/kg prednisolone per day	Yes	202	NMEM
10	English springer spaniel	ME	85	Ataxia	Multifocal	No	455	Focal	2 mg/kg/day prednisolone	No cytarabine	Improvement	Euthanased because of postoperative infection after stifle surgery, dog normal and on no medication	No	304	NP
11	Rhodesian ridgeback	FE	123	Normal gait	C1 to C5	Yes	89	Focal*	0·3 mg/kg/day dexa-methasone	50 mg/m² sc	Improvement	Euthanased because development of seizures, was still receiving cytarabine 50 mg/m² sc every 7 weeks	Yes	669	NP
12	Bearded collie	MN	136	Ambulatory paraparesis	Multifocal	Yes	162	No lesion visible	2 mg/kg/day prednisolone	50 mg/m² sc	Improvement	Normal dog, receiving no current treatment	No	1100	NA

Case	Breed	Gender	Age (months) at presentation	Clinical presentation	Neuro-anatomical localisation	Spinal hyper-aesthesia	CSF TNCC (cells/μL)	MRI lesion	Initial treatment	Cytosine arabinoside dose (mg/m^2), SC or CRI	Initial response to treatment	Long-term follow-up and treatment	Death or euthanaseda because of MUO	Overall ST (days)	Post-mortem examination findings
13	Boxer	ME	26	Normal gait	Multifocal	Yes	6000	Focal	2 mg/kg/day prednisolone	50 mg/m^2 sc	Improvement	Normal dog, receiving a dose of 50 mg/m^2 cytarabine sc every 9 weeks	No	1460	NA
14	Lhasa apso	MN	128	Ambulatory paraparesis	L4 to S3	Yes	1540	Multifocal	2 mg/kg/day prednisolone	50 mg/m^2 sc	Stable	Euthanased because of disease progression	Yes	33	NP
15	Chihuahua	ME	19	Ataxia	T3 to L3	Yes	9	Multifocal	0·3 mg/kg/day dexa-methasone	No cytosine arabinoside	Improvement	Normal dog, receiving no current treatment	No	635	NA
16	Cross-breed	FN	83	Ambulatory paraparesis	Multifocal	No	1230	Multifocal	0·3 mg/kg/day dexa-methasone	200 mg/m^2 CRI	Improvement	Euthanased because of acute deterioration, was still receiving a dose of 2 mg/kg prednisolone every day, combined with a dose of 2 mg/kg azathioprine	Yes	93	NP
17	French bulldog	ME	13	Ambulatory paraparesis	T3 to L3	No	250	Multifocal	2 mg/kg/day prednisolone	No cytosine arabinoside	Improvement	Normal dog, receiving no current treatment	No	791	NA
18	Maltese terrier	FN	104	Ataxia	Multifocal	Yes	95	Focal	0·3 mg/kg/day dexa-methasone	50 mg/m^2 sc	Improvement	Normal dog, still receiving doses of 1 mg/kg of prednisolone per day and 50 mg/m^2 cytarabine sc every 4 weeks	No	577	NA
19	Jack Russell terrier	FN	56	Non-ambulatory tetraparesis	C6 to T2	Yes	2690	Focal*	0·5 mg/kg/day dexa-methasone	No cytosine arabinoside	Dog never recovered from general anaesthesia for MRI	Dog never recovered from GA	Yes	0	GMEM
20	French bulldog	ME	10	Non-ambulatory paraparesis	T3 to L3	Yes	43	Focal	0·3 mg/kg/day dexa-methasone	50 mg/m^2 sc	Improvement	Ataxia and ambulatory paraparesis, still receiving 0·5 mg/kg of prednisolone every other day and cytarabine 50 mg/m^2 every 5 weeks	No	90	NP
21	West Highland White terrier	FE	103	Non-ambulatory tetraparesis	Multifocal	Yes	1980	Multifocal	0·3 mg/kg/day dexa-methasone	50 mg/m^2 sc	Improvement	Normal dog, receiving a dose of 5 mg/kg/day cyclosporine	No	210	NA

FE female entire, FN female neutered, ME male entire, MN male neutered, CSF cerebrospinal fluid, TNCC total nucleated cell count, sc subcutaneous, CRI constant rate infusion, NA not applicable, NP not performed, GME granulomatous meningoencephalomyelitis, NME necrotising meningoencephalomyelitis, * lesion(s) visible on intracranial images without presence of intracranial signs on neurological examination

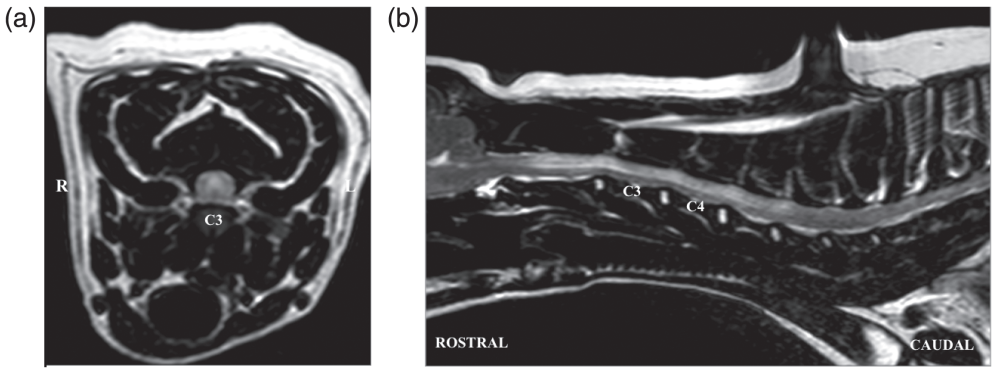

FIG 1. T2W transverse (a) MR image of the vertebral column and spinal cord at the level of C3, and mid sagittal (b) MR image of the cervical and cranial thoracic vertebral column and spinal cord of a 56-month-old Jack Russell terrier. There is a large, ill-defined, intramedullary hyperintensity extending from cranial C2 to cranial C6

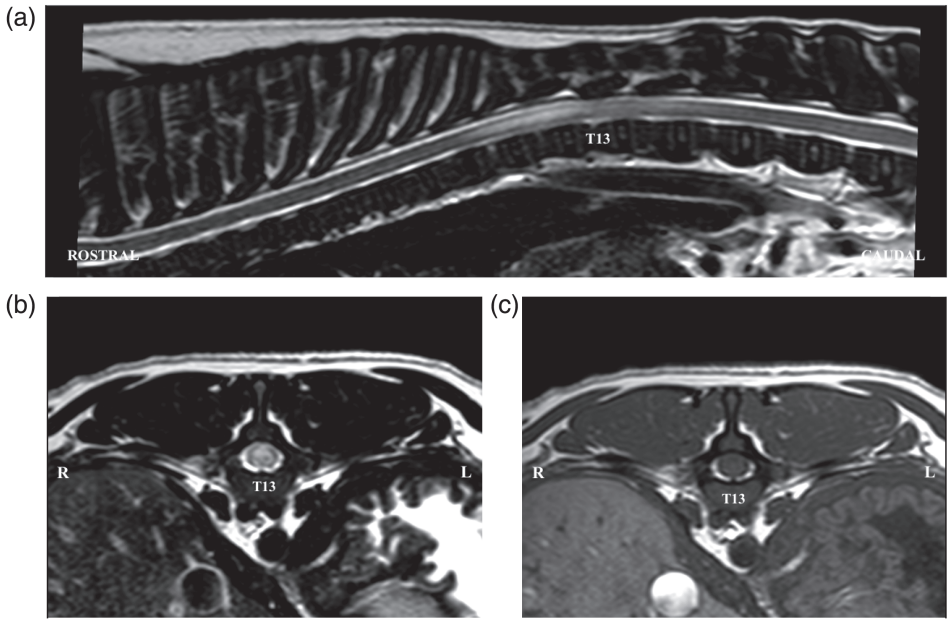

FIG 2. T2W sagittal (A) and transverse (B,C), and T1W transverse (C) images of the vertebral column and associated spinal cord of a 13-month-old French bulldog. There is a large, ill-defined, intramedullary lesion that is hyperintense on T2W images and isointense on T1W images. The lesion extends from mid T10 to caudal L1

contrast enhancement. In two dogs (10%) intracranial images were contained within the field of view of the cervical spinal cord images (T2W transverse and sagittal images), revealing multiple T2W hyperintensities in the forebrain and/or brainstem. Neither of those dogs had clinical or neurological signs of intracranial involvement at time of diagnosis. The first dog, a 56-month-old Jack Russell terrier, did not recover from general anaesthesia after diagnostic procedures, and full necropsy revealed GME. The second dog, a 123-month-old Rhodesian ridgeback, developed seizures 669 days after diagnosis and was euthanased without further investigations.

Treatment and outcome

As required by the inclusion criteria, outcome was available in all dogs. As described above, one dog did not recover from general anaesthesia for MRI of the spinal cord, and was censored for survival analysis. Mean duration of hospitalisation was five days (ranging from 1 to 19 days), with 17 dogs (81%) showing improvement in neurological status within that period. One dog (5%) remained neurologically stable (no improvement nor deterioration), and three dogs (14%) showed deterioration of their neurological status. All dogs were treated with immunosuppressive doses of glucocorticosteroids immediately after diagnosis. This consisted doses of 0·3 to 0·5 mg/kg/day dexamethasone in nine dogs (43%) iv and 2 to 4 mg/kg/day oral prednisolone in 12 dogs (57%). Fourteen dogs (67%) received additional treatment with cytosine arabinoside as a constant rate infusion (CRI) of 200 mg/m^2 over eight hours in one dog (7%) and as four subcutaneous (SC) injections of 50 mg/m^2 every 12 hours for two consecutive days in 13 dogs (93%).

Twenty dogs (95%) survived to discharge. Of these dogs, nine dogs (45%) were still alive at time of data capture. Of these nine dogs, eight were neurologically normal according to the follow-up information and one dog still showed ataxia and ambulatory

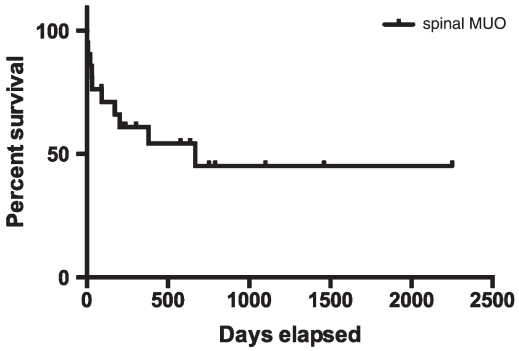

FIG 3. Kaplan-Meier survival curve for overall survival in dogs diagnosed with spinal MUO. Results were censored for dogs that were still alive at time of data capture and dogs that died because of unrelated causes (dash marks)

paraparesis. Of the eight normal dogs, two were still receiving a dose of 5 mg/kg cyclosporine every 24 hours, one was receiving a dose of 50 mg/m^2 cytosine arabinoside every 12 hours for two consecutive days every nine weeks, one was receiving a dose of 0·2 mg/kg prednisolone every 24 hours, one was receiving doses of 1 mg/kg prednisolone every 24 hours and 50 mg/m^2 cytosine arabinoside every 12 hours for two consecutive days every four weeks, and three dogs were not receiving any treatment at time of data capture. The dog that was still showing neurological abnormalities was receiving doses of 0·5 mg/kg prednisolone every other day and 50 mg/m^2 cytosine arabinoside every 12 hours for two consecutive days every 5 weeks.

For the 11/20 dogs (55%) that were dead at the time of data capture, three had died or were euthanased because of disease progression, six were euthanased because of acute neurological deterioration after initial neurological improvement and two were euthanased because of unrelated causes (complications after stifle surgery and development of aggression). Dogs that showed acute neurological deterioration after initial improvement did so within a median of 171 days after diagnosis (ranging from 30 to 669 days). Of those six dogs, one showed acute deterioration after discontinuation of prednisolone treatment and five were still receiving treatment doses of 1 mg/kg prednisolone every 24 hours, 0·5 mg/kg prednisolone every 24 hours, 2 mg/kg prednisolone every 24 hours and 2 mg/kg azathioprine every 24 hours or 50 mg/m^2 cytosine arabinoside every 12 hours for two consecutive days every seven weeks. Overall, we can conclude that 10/21 dogs (48%) died or were euthanased because of MUO.

Overall, the MST was 669 days (ranging from 1 to 2250 days) (Fig 3). Confirmation from post-mortem examination was available in three dogs, revealing GME in two and necrotising meningomyelitis in one dog. All clinical data are shown in Tables 1 and 2.

Table 2. Summary of the most important demographic, treatment and outcome data in dogs diagnosed with spinal MUO

Variable	Number (%) or median (IQR)
Signalment	
Age (months)	56 (10 to 128)
Male/female	13 (62%)/8 (38%)
Duration of clinical signs prior to diagnosis (days)	8 (1 to 90)
Onset of neurological signs	
Peracute	1 (5%)
Acute	9 (43%)
Chronic	11 (52%)
Neurological examination	
Focal/ multifocal lesion	13 (62%)/ 8 (38%)
Focal lesion localisation	
C1 to C5	3 (23%)
C6 to T2	2 (15%)
T3 to L3	6 (47%)
L4 to S3	2 (15%)
Neurological grade	
Grade 0	0
Grade 1	2 (10%)
Grade 2	14 (67%)
Grade 3	5 (24%)
Grade 4	0
Grade 5	0
Pain on spinal palpation	15 (71%)
Urinary retention	2 (10%)
Urinary and faecal incontinence	2 (10%)
CSF examination	
TNCC (cells/mm^3)	209 (6 to 6000)
TP concentration (g/L)	1·67 (0·21 to 16·3)
Treatment	
Glucocorticoids	21 (100%)
IV dexamethasone	9 (43%)
Oral prednisolone	12 (57%)
Cytosine arabinoside	14 (67%)
CRI	1 (7%)
SC injections	13 (93%)
Outcome	
Survival to discharge	20 (95%)
Alive at time of data capture	9 (45%)

IQR interquartile range, CSF cerebrospinal fluid, TNCC total nucleated cell count, TP total protein, IV intravenous, CRI constant range infusion, SC subcutaneous

DISCUSSION

This study evaluated the clinical presentation, diagnostic findings and long-term survival in 21 dogs diagnosed with presumptive spinal MUO. Dogs had a median age of five years at time of diagnosis. A lesion affecting the T3 to L3 spinal cord segments resulting in ambulatory paraparesis was the most common clinical presentation. The overall MST was 669 days, but 48% of dogs diagnosed with spinal MUO died or were euthanased because of the disease, indicating a guarded long-term prognosis.

Pain on direct spinal palpation was present in 71% of dogs. Spinal pain may reflect the involvement of the meninges, and/or vertebrae (vertebral periosteum), and/or nerve roots or spinal nerves (Da Costa 2012). In the present study, the lesions showed meningeal contrast enhancement in 18/21 dogs, but there was no apparent association between spinal hyperaesthesia and meningeal enhancement on MRI.

MRI of the spinal cord revealed no lesion on sagittal T2W and T1W images in 10% of dogs (n=2), which appears similar to the 7% described for the brain in dogs with MUO (Granger *et al.* 2010). In the retrospective study of Griffin *et al.* (2008), only one dog with meningomyelitis had MRI performed, revealing

no abnormalities. Based on these findings, MUO cannot be ruled out based on unremarkable MRI findings. The first dog was a 42-month-old bullmastiff with a 1-month history of slowly progressive T3 to L3 spinal cord lesion. After diagnostic procedures, the dog was treated with oral prednisolone but continued to deteriorate and was euthanased after 6 days. No post-mortem examination was performed. The second dog was a 136-month-old bearded collie with a 1-week history of a progressive multifocal spinal cord neuroanatomical localisation (T3 to S3 spinal cord lesion). The dog showed improvement on treatment with prednisolone and cytosine arabinoside (see Table 1) after diagnostic investigations, and was still alive without current treatment 1100 days after diagnosis. Both dogs had inflammatory CSF analysis (increased TNCC and TP concentration). For both dogs, vascular, degenerative or neoplastic spinal cord lesions cannot be excluded. As both dogs had a progressive disease course, a vascular (ischaemic) lesion seemed less likely. A neoplastic lesion cannot be excluded, although this seems rather unlikely in the bullmastiff considering his very young age. The second dog had a lymphocytic pleocytosis on CFS analysis, but no signs of lymphoma on microscopical examination, although no specific test for clonality was performed.

All MRI-observed lesions were extensive, ill-defined, intramedullary, hyperintense on T2W images and isointense on T1W images. Other spinal conditions, including acute non-compressive nucleus pulposus extrusions (ANNPE) and ischaemic myelopathy (IM), are also associated with intraparenchymal hyperintensities on MRI. However, these conditions are associated with other clinical and additional MRI characteristics, which could potentially aid in differentiating between these conditions (Cardy *et al*. 2015, Fenn *et al*. 2016). According to Cardy *et al*. (2015), in dogs presenting with spinal cord dysfunction, IM [most commonly fibrocartilagenous embolic myelopathy (FCEM)] and ANNPE are typically characterised by a peracute onset of non-progressive clinical signs and affected dogs do not commonly demonstrate overt spinal hyperaesthesia at time of admission. This is in contrast with the clinical presentation of dogs with spinal MUO, which was characterised by an acute onset of progressive and mainly symmetrical neurological deficits, with pain on spinal palpation or manipulation in 86% of dogs (Cardy *et al*. 2015), which is comparable with the 71% of dogs presenting with spinal hyperaesthesia in the current study. Although CSF analysis in dogs with IM is most often within normal limits, affected dogs can demonstrate an increased TP concentration and mild neutrophilic or mixed cell pleocytosis with a median TNCC of 12 cells/μL (De Risio *et al*. 2007). A marked pleocytosis with a median TNCC of 209 cells/mm^3 was seen in the current study, although this conclusion should be treated with caution because CSF pleocytosis was one of the inclusion criteria. To conclude, the presentation of a dog with an acute or chronic onset of a progressive and painful T3 to L3 myelopathy in combination with an extensive, ill-defined, intramedullary lesion plus parenchymal and/or meningeal contrast enhancement on MRI, and marked pleocytosis on CSF analysis, can be presumptively diagnosed with spinal MUO. The importance of differentiating between these conditions is highlighted by the differences in treatment and prognosis between dogs with presumptive MUO and dogs with ANNPE or IM.

A previous study demonstrated that short tau inversion recovery (STIR) hyperintensities in the cervical epaxial musculature of dogs with meningoencephalomyelitis had a sensitivity of 78% and a specificity of 92% in predicting inflammatory CSF results (Eminaga *et al*. 2013). In the current study, STIR images were unfortunately only available in 3/21 cases. Adding this sequence to the protocol in dogs with presence of a focal or multifocal, ill-defined T2W intramedullary hyperintensity might be considered in the future.

Several studies have evaluated survival times of dogs diagnosed with MUO (Granger *et al*. 2010, Coates & Jeffery 2014). Overall, dogs with MUO appear to have a guarded prognosis. A large meta-analysis of dogs with MUO revealed an overall reported MST of 240 to 590 days in 96 dogs treated with corticosteroids plus any other immunosuppressive protocol, compared to a MST of 28 to 357 days for 43 dogs receiving corticosteroids alone (Granger *et al*. 2010). In the current study, dogs with presumptive spinal MUO had a MST of 669 days (2 years), but ultimately, 48% of dogs died or were euthanased because of the disease, indicating a more guarded long-term prognosis.

Limitations of this study are the small sample size and retrospective character, which limited standardisation of patient assessment and treatment. Although all dogs were treated with glucocorticosteroids, it cannot be excluded that specific differences in treatment may have influenced outcomes. Despite including cases over a relative large period and from a busy referral hospital, only 21 dogs were found through our record search. This could indicate that spinal MUO should be considered a rare disorder, which is in agreement with previous reports (Cardy *et al*. 2015), suggesting that MUO represents approximately 6% of all spinal disorders in dogs.

Presumptive spinal MUO can be diagnosed in any type of dog of any age that is presented with signs of acute or chronic, possibly painful, myelopathy. Although clinical signs can vary, affected animals most typically present with ambulatory paraparesis and ataxia, localising to T3 to L3 spinal cord segments. MRI typically reveals an extensive, ill-defined and intramedullary lesion that appears hyperintense on T2W images and isointense on T1W images. Most lesions showed parenchymal contrast enhancement and/or enhancement of the overlying meninges on post-contrast T1W images which can possibly differentiate dogs with MUO from other more common spinal diseases. In 10% of cases, no lesion was visible on sagittal T2W and T1W images. Almost 50% of dogs died or were euthanased because of MUO, with a MST of 669 days.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of this paper.

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