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.

INTRODUCTION

Pure myelitis (inflammation of spinal cord parenchyma) or meningo(myelitis (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, Catterbr, Angiostrongylus vasorum) and algae (Prototheca wickerhamii, Prototheca zopfi) are known causes for meningo(myelitis in dogs and cats, with or without concurrent intracranial signs (Griffin et al. 2008, Parry...
et al. 2009, Cebi 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 et al. 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 meningoencephalitis, 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 meningo(myelo)myelitis 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 meningo(myelo)myelitis. 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/intradural 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 cerebrovascular hyperesthesia. CSF analysis in SRMA typically reveals a predominantly neutrophilic pleocytosis (Dewey et al. 2016). Dogs with histopathological confirmation of the disease [granulomatous meningitis(encephalo)myelitis (GME) or necrotising meningitis(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/mm³. 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 without 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 (Integra, Philips Medical Systems, Eindhoven, the Netherlands) and all images were reviewed by the corresponding author using Osirix Dicom viewer (Osirix Foundation, V5.5.2 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<0.05 were considered significant. Survival analysis was performed using both a Log-rank (Mantel-Cox) and Gehan-Breslow-Wilcoxon test, resulting in median survival time (MST) calculated 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=0.075). 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/mm³ (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>
<thead>
<tr>
<th>Case</th>
<th>Breed</th>
<th>Gender</th>
<th>Age (months) at presentation</th>
<th>Clinical presentation</th>
<th>Neuro-anatomical localisation</th>
<th>Spinal hyperesthesia</th>
<th>CSF TNCC (cells/µL)</th>
<th>MRI lesion</th>
<th>Initial treatment</th>
<th>Cytosine arabinoside dose (mg/m²), SC or CRI</th>
<th>Initial response to treatment</th>
<th>Long-term follow-up and treatment</th>
<th>Death or euthanased because of MUO</th>
<th>Overall ST (days)</th>
<th>Post-mortem examination findings</th>
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<tbody>
<tr>
<td>1</td>
<td>Akita</td>
<td>FE</td>
<td>36</td>
<td>Non-ambulatory paraparesis</td>
<td>Multifocal</td>
<td>Yes</td>
<td>1740</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Euthanased because of acute deterioration after discontinuation of prednisolone treatment</td>
<td>Yes</td>
<td>380</td>
<td>NA</td>
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<tr>
<td>2</td>
<td>Rottweiler</td>
<td>ME</td>
<td>123</td>
<td>Ataxia</td>
<td>T3 to L3</td>
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<td>209</td>
<td>Focal</td>
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<td>Deterioration</td>
<td>Euthanased because of disease progression</td>
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<td>20</td>
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<td>Bull mastiff</td>
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<td>T3 to L3</td>
<td>Yes</td>
<td>6</td>
<td>No lesion visible Focal</td>
<td>Deterioration</td>
<td>Euthanased because of disease progression</td>
<td>Yes</td>
<td>6</td>
<td>NA</td>
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<td>Labrador</td>
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<td>105</td>
<td>Ambulatory paraparesis</td>
<td>L4 to S3</td>
<td>Yes</td>
<td>123</td>
<td>Focal</td>
<td>0·3 mg/kg/day dexamethasone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Euthanased because of acute deterioration, was still receiving a dose of 1 mg/kg prednisolone every day</td>
<td>Yes</td>
<td>30</td>
<td>NA</td>
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<tr>
<td>5</td>
<td>Jack Russell terrier</td>
<td>MN</td>
<td>89</td>
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<td>T3 to L3</td>
<td>No</td>
<td>200</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone No cytosine arabinoside</td>
<td>Improvement</td>
<td>Normal dog, still receiving a dose of 0·2mg/kg/day prednisolone</td>
<td>No</td>
<td>237</td>
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<tr>
<td>6</td>
<td>Lhasa apso</td>
<td>FE</td>
<td>48</td>
<td>Ambulatory tetraparesis</td>
<td>C1 to C5</td>
<td>Yes</td>
<td>900</td>
<td>Focal</td>
<td>4 mg/kg/day prednisolone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Euthanased because of acute deterioration, was still receiving a dose of 0·5 mg/kg prednisolone every day</td>
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<td>171</td>
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<tr>
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<td>50</td>
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<td>O6 to T2</td>
<td>Yes</td>
<td>5</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Normal dog, receiving a dose of 5 mg/kg/day ciclosporine</td>
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<td>Giant schnauzer</td>
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<td>Non-ambulatory paraparesis</td>
<td>Multifocal</td>
<td>No</td>
<td>1345</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Euthanased because of agression, was only receiving cytosine arabinoside every 5 weeks</td>
<td>No</td>
<td>752</td>
<td>NP</td>
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<td>Yorkshire terrier</td>
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<td>Ambulatory tetraparesis</td>
<td>C1 to C5</td>
<td>Yes</td>
<td>7</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone No cytosine arabinoside</td>
<td>Improvement</td>
<td>Euthanased because of acute deterioration, was still receiving a dose of 1 mg/kg prednisolone per day</td>
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<td>English springer spaniel</td>
<td>ME</td>
<td>85</td>
<td>Ataxia</td>
<td>Multifocal</td>
<td>No</td>
<td>455</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone No cytarabine</td>
<td>Improvement</td>
<td>Euthanased because of postoperative infection after stifle surgery, dog normal and on no medication</td>
<td>No</td>
<td>304</td>
<td>NP</td>
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<td>Rhodesian ridgeback</td>
<td>FE</td>
<td>123</td>
<td>Normal gait</td>
<td>C1 to C5</td>
<td>Yes</td>
<td>89</td>
<td>Focal*</td>
<td>0·3 mg/kg/day dexamethasone 50 mg/m² sc</td>
<td>Improvement</td>
<td>Euthanased because of development of seizures, was still receiving cytarabine 50 mg/m² sc every 7 weeks</td>
<td>Yes</td>
<td>669</td>
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<td>Yes</td>
<td>162</td>
<td>No lesion visible Focal</td>
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<td>Normal dog, receiving no current treatment</td>
<td>No</td>
<td>1100</td>
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<tr>
<td>Case</td>
<td>Breed</td>
<td>Gender</td>
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<td>Clinical presentation</td>
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<td>Spinal hyper-aesthesia</td>
<td>CSF TNCC (cells/µL)</td>
<td>MRI lesion</td>
<td>Initial treatment</td>
<td>Cytosine arabinoside dose (mg/m²), SC or CRI</td>
<td>Initial response to treatment</td>
<td>Long-term followup and treatment</td>
<td>Death or euthanased because of MUO</td>
<td>Overall ST (days)</td>
<td>Post-mortem examination findings</td>
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<td>Normal gait</td>
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<td>6000</td>
<td>Focal</td>
<td>2 mg/kg/day prednisolone</td>
<td>50 mg/m² SC</td>
<td>Improvement</td>
<td>Normal dog, receiving a dose of 50mg/m² cytarabine sc every 9 weeks</td>
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<td>14</td>
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<td>MN</td>
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<td>1540</td>
<td>Multifocal</td>
<td>2 mg/kg/day prednisolone 0-3 mg/kg/day dexamethasone</td>
<td>50 mg/m² SC 200mg/m² CRI</td>
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<td>Euthanased because of disease progression</td>
<td>Yes</td>
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<td>ME</td>
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<td>9</td>
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<td>0-3 mg/kg/day dexamethasone No cytosine arabinoside</td>
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<td>Improvement</td>
<td>Normal dog, receiving no current treatment</td>
<td>No</td>
<td>635 NA</td>
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<td>16</td>
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<td>No</td>
<td>1230</td>
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<td>0-3 mg/kg/day dexamethasone</td>
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<td>Improvement</td>
<td>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</td>
<td>Yes</td>
<td>93 NP</td>
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<td>250</td>
<td>Multifocal</td>
<td>2 mg/kg/day prednisolone No cytosine arabinoside</td>
<td>50 mg/m² SC 0-3 mg/kg/day dexamethasone</td>
<td>Improvement</td>
<td>Normal dog, receiving no current treatment</td>
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<td>Yes</td>
<td>95</td>
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<td>Improvement</td>
<td>Normal dog, still receiving doses of 1 mg/kg of prednisolone per day and 50 mg/m² cytarabine sc every 4 weeks</td>
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<tr>
<td>19</td>
<td>Jack Russell terrier</td>
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<td>Yes</td>
<td>2690</td>
<td>Focal *</td>
<td>0-5 mg/kg/day dexamethasone No cytosine arabinoside</td>
<td>Dog never recovered from general anaesthesia for MRI</td>
<td>Improvement</td>
<td>Dog never recovered from GA</td>
<td>Yes</td>
<td>0 GMEM</td>
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<tr>
<td>20</td>
<td>French bulldog</td>
<td>ME</td>
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<td>Non-ambulatory paraparesis</td>
<td>T3 to L3</td>
<td>Yes</td>
<td>43</td>
<td>Focal</td>
<td>0-3 mg/kg/day dexamethasone</td>
<td>50 mg/m² SC</td>
<td>Improvement</td>
<td>Ataxia and ambulatory paraparesis, still receiving 0-5 mg/kg of prednisolone every other day and cytarabine 50 mg/m² every 5 weeks</td>
<td>No</td>
<td>90 NP</td>
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<td>West Highland White terrier</td>
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<td>103</td>
<td>Non-ambulatory tetraparesis</td>
<td>Multifocal</td>
<td>Yes</td>
<td>1980</td>
<td>Multifocal</td>
<td>0-3 mg/kg/day dexamethasone</td>
<td>50 mg/m² SC</td>
<td>Improvement</td>
<td>Normal dog, receiving a dose of 5mg/kg/day cyclosporine</td>
<td>No</td>
<td>210 NA</td>
<td></td>
</tr>
</tbody>
</table>

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.
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 the 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 of 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/m² over eight hours in one dog (7%) and as four subcutaneous (SC) injections of 50 mg/m² 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 the 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
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/m² cytosine arabinoside every 12 hours for two consecutive days every nine weeks, one was receiving doses of 1 mg/kg prednisolone every 24 hours and 50 mg/m² 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/m² 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/m² 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.

**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 (ANNEP) 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 ANNEP 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/mm³ 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 ANNEP 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.

References