ORIGINAL ARTICLE

Magnetic resonance imaging findings in dogs with steroid-responsive meningitis-arteritis in the UK and their clinical significance: 53 cases (2013-2021)

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Objectives: To describe the MRI findings in a UK referral population of dogs with steroid-responsive meningitis-arteritis and to determine if they were associated with any specific clinical features or outcomes.

Materials and Methods: We performed a multi-centre retrospective case series of dogs diagnosed with steroid-responsive meningitis-arteritis in the UK that underwent MRI. Blinded consensus review of the MRI studies was performed and the findings described. The presence or absence of specific MRI abnormalities were analysed for significant associations with presenting signs, results of investigations or case outcomes.

Results: Fifty-three dogs were included. The most common MRI findings were paravertebral muscle changes (30/53; 56.6%), meningeal contrast enhancement (13/41; 31.7%) and spinal cord parenchymal T2-W hyperintensity (15/53; 28.3%). Haemorrhage was observed in five of 53 (9.4%) cases – three intradural-extramedullary, one intramedullary and one extradural. Following binary logistic regressions, T2-W spinal cord parenchymal hyperintensity had a significant positive association with paresis/paralysis (odds ratio 14.86, 95% confidence interval 1.42 to 154.99) as did haemorrhage (odds ratio 16.12, confidence interval 2.05 to 126.73). Fifty-two (98.1%) dogs survived to discharge. Relapse occurred in nine of 29 (31.0%) dogs with sufficient follow-up, and no MRI finding had a significant relationship with its occurrence.

Clinical Significance: Magnetic resonance imaging findings for steroid-responsive meningitis-arteritis can be severe and extensive, as can the clinical presentation. The presence of paresis/paralysis should raise concern for haemorrhage, though most dogs still have a good prognosis.

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INTRODUCTION

Steroid-responsive meningitis-arteritis (SRMA) is a systemic immune-mediated disease, causing inflammatory lesions in the meninges, predominantly of the spinal cord and their arteries, although lesions have been documented in the coronary, mediastinal and thyroid arteries (Bathen-Noethen et al., 2008; Cizinauskas et al., 2000; Scott-Moncrieff et al., 1992; Tipold & Schatzberg, 2010; Tipold & Stein, 2010). An immune-mediated pathogenesis is suspected based on marked increases in acute phase proteins and other factors (e.g., immunoglobulin A, toll-like receptor expression patterns) associated with a likely Th-2 mediated systemic immune response, alongside the positive response to glucocorticoid therapy (Bathen-Noethen et al., 2008; Maiolini, Carlson, Schwartz, et al., 2012a; Maiolini, Carlson, & Tipold, 2012b; Schwartz et al., 2008, 2011; Tipold & Schatzberg, 2010).

SRMA typically affects young dogs, with a peak age of 6 to 18 months, although older dogs can be affected (Biedermann et al., 2016; Cizinauskas et al., 2000; Tipold & Schatzberg, 2010). It is the most common diagnosis in young pyrexic dogs being presented to UK referral institutions (Black et al., 2019). Acute and chronic forms are described (Tipold & Jaggy, 1994; Tipold & Schatzberg, 2010). The more common acute form is typified by spinal hyperaesthesia, cervical rigidity, stilted gait and pyrexia (Cizinauskas et al., 2000; De Strobel et al., 2019; Gonçalves et al., 2022; Grapes et al., 2020). Spinal pain aside, neurological examination is typically unremarkable (Schwartz et al., 2010). Cerebrospinal fluid (CSF) analysis usually reveals a non-degenerate neutrophilic pleocytosis (Tipold & Jaggy, 1994; Trevail & Behr, 2014). Dogs with severe, acute myelopathic presentations are reported, often with evidence of haemorrhage or diffuse central nervous system (CNS) suppurative inflammation (Brocal et al., 2017; Wang-Leandro et al., 2017; Wrzosek et al., 2009; Zilli et al., 2021). The chronic form has been associated with relapses or untreated disease, potentially more significant neurological abnormalities, and variable CSF results, with a mononuclear or mixed pleocytosis reported (Tipold & Jaggy, 1994; Trevail & Behr, 2014).

Definitive SRMA diagnosis requires histopathological examination (Gonçalves et al., 2022; Lowrie et al., 2009). Most cases are presumptively diagnosed based on signalment, presentation and CSF analysis, alongside response to therapy (Gonçalves et al., 2022; Lau et al., 2019; Lowrie et al., 2009; Maiolini, Carlson, Schwartz, et al., 2012a; Tipold & Jaggy, 1994; Trevail & Behr, 2014). A diagnosis is frequently made without MRI, but it may be performed due to atypical presentations or institutional preference (Fuchs et al., 2000; Lau et al., 2019; Tipold & Stein, 2010). Findings on MRI have been infrequently reported, although abnormalities appear common (74% to 98.6% of cases), in particular meningeal, articular facet synovium and paravertebral muscle contrast enhancement, as well as cervical spinal cord parenchymal changes (Lau et al., 2019; Remelli et al., 2022). Previous studies have been based outside the UK, and there is no current data to suggest if MRI findings offer any prognostic or clinical significance.

The objectives of this study were to describe the MRI findings of dogs diagnosed with SRMA, and to determine if any significant relationships exist between these findings and the clinical features or patient outcomes. We hypothesised that dogs with MRI lesions would have a longer disease course, increased mortality and a higher incidence of relapse.

MATERIALS AND METHODS

Study design and inclusion criteria

Records of six UK referral hospitals were searched for dogs diagnosed with SRMA. Inclusion criteria included dogs with a presumptive diagnosis of SRMA based on signalment, examination findings, evidence of systemic inflammation, pleocytosis on CSF analysis and response to therapy where available (i.e., an improvement in clinical signs with glucocorticoid or immunosuppressive therapy). Additionally, MRI performed at the time of investigation had to be available for review. A pleocytosis was defined as a CSF (cisternal or lumbar) total nucleated cell count (TNCC) >5 cells/μL. Systemic inflammation was defined by the presence of one of the following: increased C-reactive protein (CRP) concentration (>10 mg/L), pyrexia (recorded in the clinical history text or documented body temperature >39.0°C) or documented peripheral neutrophilia. A histopathological diagnosis of SRMA also allowed inclusion regardless of other results.

Data extracted

Data were collected relating to signalment, presenting clinical signs, neurological examination, clinicopathological results, treatment and outcome where available. Remission was defined as the absence of clinical signs while receiving treatment, and resolution the absence of signs following treatment discontinuation. Relapse was defined as the recurrence of clinical signs similar to those of initial presentation, and a positive response to the re-institution of therapy.

MRI studies

Six systems were used to acquire MRIs – four high-field and two low-field (centre 1 = 1.5 T Philips Achieva, Philips, Best, Netherlands; centre 2 = Aperto Lucent 0.4 T, Hitachi, Tokyo, Japan; centres 3 and 4 = Intera 1.5 T, Phillips, Best, Netherlands; centre 5 = HDE 1.5 T General Electric, Boston, USA; centre 6 = Vet-MR Grande 0.27 T, Esaote, Genoa, Italy). Contrast administered was gadolinium-based. Patients without contrast administration were not excluded.

Image review was performed on a computer workstation (iMac, Retina 5K, 27-in., 2019, Apple, California, USA) using open-source viewing software (Horos v4.0.0 RC5). Each study was assessed by a board-certified specialist in diagnostic imaging and a board-certified specialist in veterinary neurology in collaboration, blinded to all other case details, with a consensus recorded. Evaluation included both the CNS region included in the examination and the surrounding structures (including paravertebral muscles and lymph nodes in the field of view). Structures were assessed subjectively for changes in size, signal intensity, contrast enhancement or evidence of haemorrhage (based on the presence of a magnetic susceptibility artefact on the T2* gradient echo

[T2*GE] or susceptibility-weighted imaging sequences within the soft tissues of the cranial cavity or vertebral canal). The location (cranial, cervical, thoracic and lumbar), distribution (focal, multifocal and diffuse) and subjective severity (mild, moderate and severe; with the most severe recorded if borderline) of abnormalities were recorded. The presence and location of any lymphadenomegaly were recorded. Where anatomical regions were absent from the study, these were excluded from analysis.

Patient and MRI data were recorded and analysed using Microsoft Excel (version 16.56). Continuous variables were summarised as medians and ranges, and categorical variables as frequencies and percentages.

Data analysis

Variables relating to the presentation or clinicopathological results were chosen for comparison with the presence/absence of MRI spinal cord abnormalities, meningeal contrast enhancement, haemorrhage or paravertebral muscle changes. The variables chosen were duration of clinical signs, body temperature, peripheral neutrophil count, CRP concentration, cisternal CSF TNCC, lumbar CSF TNCC, and the presence/absence of pyrexia, increased creatine kinase (CK) activity, myelopathic signs, paresis/paralysis specifically, disease relapse and survival to discharge. Imaging variables were also compared between high- and low-field MRI studies to identify potentially significant differences.

The presence or absence of MRI findings was compared to binary categorical variables using Fisher's exact tests and to continuous variables using Kruskal-Wallis tests adjusted for ties. Following initial screening with these methods, stepwise binary logistic regressions were performed for any relationships with a P-value <0.20 and based on a sample size of at least 40. These regressions all included a fixed term indicating a low- or high-field MRI in every model, to check for any confounding effect of this. Statistical significance was taken as $P < 0.05$. Statistical analysis was performed using Minitab v19.

RESULTS

Signalment

Fifty-three dogs fulfilled the inclusion criteria. The median age at diagnosis was 12 months (range 5 to 52 months). Twenty-seven (50.9%) dogs were male (10 neutered) and 26 (49.1%) were female (12 neutered, one not recorded). The most frequent breed was crossbreed (15) followed by beagle (six), boxer (four), springer spaniel (four), Labrador retriever (three), whippet (three), Weimaraner (three), golden retriever (three), lurcher (two), cocker spaniel (two) and one each of coton de Tulear, Jack Russell terrier, bearded collie, miniature schnauzer, border collie, Irish setter, English setter and Chihuahua.

Clinical presentation

Data relating to clinical signs duration were available for 44 dogs (83.0%). The median duration of signs was 5 days (range 1 to 300 days). In nine (20.5%) of the 44 dogs, signs had been present for at least 30 days, consistent with a chronic disease course. Pyrexia was reported in 45 dogs (84.9%); however, only 37 dogs (69.8%) had a rectal temperature recorded (median 39.6°C, range 37.7 to 40.5°C). Clinical findings are summarised in Table 1.

Physical examination findings

Forty-nine dogs (92.4%) had cervical hyperaesthesia and 24 (45.3%) had other spinal hyperaesthesia (three thoracic, 10 thoracolumbar, three lumbar, two lumbosacral and six diffuse), three of which did not have cervical hyperaesthesia. Eighteen dogs (34.0%) were presented with cervical hyperaesthesia only and no neurological abnormalities. One dog (1.9%) was presented without spinal hyperaesthesia. Aside from spinal hyperaesthesia, 18 dogs (34.0%) had other abnormalities noted on neurological assessment. Seven dogs (13.2%) had paresis or paralysis, and eight additional dogs (15.1%) had other myelopathic signs (ataxia, reduced postural reactions or reduced spinal reflexes). One dog had left-sided Horner's syndrome, reduced gag reflex, cervical hyperaesthesia and pyrexia; phenylephrine testing was consistent with a first-order neuron lesion.

Clinicopathologic results

Complete blood count was performed in all dogs, but full haematological data were only available for 42 dogs (79.2%), with partial data available for three more (Table S1). Thirty-eight of 45 dogs (84.4%) had an increased neutrophil count, with neutrophilia reported in the history of six more, for a total of 44 of 53 dogs (83.0%). The median neutrophil count was 17.13×10^9/L (range 4.52 to 26.45×10^9/L).

Serum biochemistry was performed in 48 dogs (90.6%), with full results available for 36 (67.9%) (Table S2). Increased aspartate aminotransferase activity was noted in six of 19 (31.6%), and increased CK activity in 14 of 31 dogs (45.1%; median 206 U/L, range 45 to 1139 U/L) where measured. Serum CRP concentration was increased in all 28 dogs where measured (median 67.5 mg/L, range 19 to 234 mg/L).

Fifty-two dogs (98.1%) had CSF analysis; one dog was diagnosed post-mortem and CSF results were unavailable. Cerebellomedullary cistern CSF samples were obtained in 47 of 52 dogs (90.3%), 13 (25.0%) had lumbar sampling and eight (15.4%) had sampling from both locations. Results are outlined in Table 2. Fifty-one of 52 dogs (98.1%) had a pleocytosis. One dog had normal CSF results at the time of MRI, but 4 weeks later had repeat CSF analysis due to lack of clinical improvement, showing neutrophilic pleocytosis (TNCC 9 cells/μL, 85% neutrophils, protein concentration 0.23 g/L), leading to its inclusion. The initial (normal) result obtained at the time of MRI was used for analysis.

Infectious disease testing is summarised in Table 3. One 8-month-old dog with neck pain, a neutrophilic pleocytosis and MRI paravertebral muscle changes, had positive point-of-care (SNAP 4Dx; Idexx) and equivocal external laboratory *Ehrlichia canis* ELISA serology results. Polymerase chain reaction (PCR) was not performed. The dog showed rapid clinical improvement with glucocorticoid treatment and was treated with doxycycline to prevent immunosuppression-related recrudescence. A 13-month-old dog with chronic spinal hyperaesthesia, pyrexia, a neutrophilic pleocytosis and MRI paravertebral

Table 1. Summary of the presenting signs and findings on physical and neurological examinations

Clinical sign	Number (%)
Presenting signs	
Lethargy	47/53 (88.7)
Pyrexia	45/53 (84.9)
Hyporexia/anorexia	27/53 (50.9)
Reluctance to move	24/53 (45.3)
Stiff gait	16/53 (30.2)
Kyphosis	11/53 (20.8)
Diarrhoea	8/53 (15.1)
Tremors	6/53 (11.3)
Vomiting	5/53 (9.4)
Seizure	1/53 (1.9)
Clinical and neurological examination findings	
Spinal pain	52/53 (98.1)
Cervical	49/53 (92.5)
Thoracic	3/53 (5.7)
Thoracolumbar	10/53 (18.9)
Lumbar	3/53 (5.7)
Lumbosacral	2/53 (3.8)
Diffuse	6/53 (11.3)
Other neurological abnormalities (aside from spinal pain)	18/53 (34.0)
Paresis	5/53 (9.4)
Pelvic limbs	3/53 (5.7)
Ambulatory	2/53 (3.8)
Non-ambulatory	1/53 (1.9)
All limbs	2/53 (3.8)
Non-ambulatory	2/53 (3.8)
Paralysis	2/53 (3.8)
Pelvic limbs	2/53 (3.8)
Absent nociception	1/53 (1.9)
Ataxia	6/53 (11.3)
Pelvic limbs	3/53 (5.7)
All limbs	2/53 (3.8)
Location not recorded	1/53 (1.9)
Delayed postural reactions or hopping	8/53 (15.1)
Pelvic limbs	6/53 (11.3)
Thoracic limbs	1/53 (1.9)
Right thoracic	1/53 (1.9)
Lameness	3/53 (5.7)
Left thoracic	2/53 (3.8)
Right thoracic	1/53 (1.9)
Reduced spinal reflexes	4/53 (7.5)
Thoracic limbs	3/53 (5.7)
Right thoracic	1/53 (1.9)
Facial twitching	1/53 (1.9)
Head tilt	1/53 (1.9)
Swelling over neck	1/53 (1.9)
Poor ventilation	1/53 (1.9)
Horner's syndrome	1/53 (1.9)
Absent menace response (unilateral)	1/53 (1.9)

muscle changes demonstrated a low serum *Neospora caninum* immunofluorescent antibody test (IFAT) titre (1:200). CSF PCR was negative, and 3-week convalescent serology showed a decreased titre (1:50). The dog showed minimal improvement with dexamethasone, ciclosporin, cytarabine and clindamycin. Clinical remission occurred following further cytarabine and the addition of azathioprine.

Diagnostic imaging findings

Twenty-eight MRI studies (52.8%) were acquired with high-field systems and 25 with low-field. All studies included at least one sagittal T2-W or T2-W Dixon series. A short tau inversion recovery (STIR) sequence was performed in 41 examinations (77.4%) and a T2-W Dixon with fat suppression was performed in a further four (7.5%). Eight studies (15.1%) had T2-W and STIR sequences only (six of which were sagittal views only), and one (1.9%) had a T2-W sagittal sequence only. Fifteen studies (28.3%) included a T2*GE or susceptibility-weighted imaging sequence. T1-W sequences were performed in 44 cases (83.0%) with 40 (75.5%) also including a post-contrast T1-W series. The most included region was cervical (45/53; 84.9%), followed by the thoracic and lumbar regions (13/53; 24.5% each) and the brain (12/53; 22.6%).

The MRI findings are summarised in Table 4. Changes in the paravertebral muscles were the most common abnormality, recorded in 30 dogs (56.6%), mostly observed as hyperintensity on STIR (29/49; 59.2%) or T2-W (27/53; 50.9%) sequences (Figs 1 and 2A), as well as contrast enhancement (22/40; 55.0%). Thirty of 36 dogs (83.3%) with spinal cord or paravertebral musculature abnormalities had lesions affecting the cervical region. The second most common abnormality was meningeal contrast enhancement (13/41; 31.7%, Fig 3).

There was evidence of haemorrhage in five cases (9.4%) based on the presence of a magnetic susceptibility artefact on the T2*GE sequence – three intradural-extramedullary, one intramedullary (Fig 2B) and one extradural. Two of these were presented with paraparesis (one non-ambulatory with intramedullary haemorrhage, the other ambulatory with intradural haemorrhage), one was tetraplegic (extradural haemorrhage confined to the cervical region) and the other two demonstrated cervical hyperaesthesia and reluctance to move (both with intradural haemorrhage). There was equivocal evidence of haemorrhage in three further cases. In one, a heterogenous T2-W and T1-W signal intensity was present in the subarachnoid space, which had an irregular shape and displaced the spinal cord ventrally and to the left. This area showed inconsistent magnetic susceptibility artefact in the T2*GE sequence. In the second, T2-W and T1-W hypointense extradural material was present, suspected to represent haemorrhage; however, no T2*GE series was available for confirmation. In the third, extensive extradural T2-W and STIR hypointense material, possibly representing haemorrhage, was present in the ventral epidural space but a T2*GE was unavailable.

Of seven dogs presented with paresis or paralysis, six (85.7%) had intramedullary T2-W hyperintensity, four (57.1%) had meningeal enhancement and three (42.9%) had intramedullary contrast enhancement. Six (85.7%) had paravertebral muscle changes, none of which affected the cervical region alone. In the other eight myelopathic dogs, none had parenchymal T2-W hyperintensity or contrast enhancement, one (12.5%) had meningeal enhancement, one (12.5%) had equivocal evidence of haemorrhage and five (62.5%) had paravertebral muscle changes.

Fourteen dogs (26.4%) had normal MRI studies and three more (5.7%) had lymphadenomegaly only. Fourteen dogs (26.4%) had paravertebral muscle changes only. These 31 cases (58.5%) together were not considered to have significant MRI spinal cord abnormalities for the purposes of further analysis.

Table 2. A summary of results of CSF analysis within the study population

Parameter	Number	Unit
Cisternal CSF ($n=47$)		
Median TNCC ($n=47$)	312 (3 to 24,000)	Cells/μL
Median total protein concentration ($n=42$)	61 (15 to 391)	mg/dL
Median neutrophil differential count ($n=31$)	70 (36 to 80)	% of cells
Neutrophilic predominance ($n=45$)	41/45 (91.1%)	Number of cases
Lumbar CSF ($n=13$)		
Median TNCC ($n=13$)	270 (9 to 6783)	Cells/μL
Median total protein concentration ($n=11$)	138 (35 to 2425)	mg/dL
Median neutrophil differential count ($n=11$)	74 (30 to 90)	% of cells
Neutrophilic predominance ($n=13$)	11/13 (84.6%)	Number of cases

CSF Cerebrospinal fluid, TNCC Total nucleated cell count

Table 3. Details of infectious disease testing performed in the study population

Infectious disease test	Number of dogs performed on, *n* (%)
Neospora caninum	35/53 (66.0)
Serology (antibody)	16/53 (30.2)
CSF PCR	15/53 (28.3)
Serology (antibody) and CSF PCR	3/53 (5.7)
Unspecified	1/53 (1.9)
Toxoplasma gondii	34/53 (64.2)
Serology (antibody)	18/53 (34.0)
CSF PCR	12/53 (22.6)
Serology (antibody) and CSF PCR	3/53 (5.7)
Unspecified	1/53 (1.9)
Ehrlichia sp.	9/53 (17.0)
Serology (antibody)	4/53 (7.5)
CSF PCR	4/53 (7.5)
Unspecified	1/53 (1.9)
Angiostrongylus vasorum (blood antigen)	6/53 (11.3)
Canine Distemper Virus (CSF PCR)	6/53 (11.3)
Bacterial meningitis (CSF culture)	6/53 (11.3)
Anaplasma sp.	5/53 (9.4)
Serology (antibody)	4/53 (7.5)
Unspecified	1/53 (1.9)
Borrelia burgdorferi (antibody serology)	4/53 (7.5)
Dirofilaria immitis (blood antigen)	4/53 (7.5)
Giardia sp. (antibody serology)	2/53 (3.8)
Leishmania infantum (antibody serology)	1/53 (1.9)

PCR Polymerase chain reaction, CSF Cerebrospinal fluid

Statistical comparisons for MRI abnormalities

When comparing clinical variables for the presence or absence of MRI spinal cord abnormalities, dogs with spinal cord abnormalities had a significantly higher cisternal CSF TNCC (median 603 cells/μL with abnormalities vs. 169 cells/μL without, P = 0.032) and a significantly higher likelihood of paresis/paralysis (31.8% with abnormalities had paresis/paralysis vs. 0.0% without, P = 0.001).

Regarding specific MRI lesions, dogs with T2-W spinal cord parenchyma hyperintensity had a significantly higher lumbar (but not cisternal) CSF TNCC (median 2027 cells/μL with vs. 65 cells/μL without, P = 0.032). Dogs with T2-W parenchymal hyperintensity and dogs with evidence of haemorrhage were both significantly more likely to have paresis/paralysis (40.0% with paresis/paralysis vs. 2.6% without, P = 0.001 and 60.0% with vs. 8.3% without, P = 0.013, respectively). Dogs with meningeal contrast enhancement had significantly higher peripheral neutrophil counts (median 20×10^9/L with vs. 15.2×10^9/L without, P = 0.019) and cisternal CSF TNCC (median 1260 cells/μL with vs. 138 cells/μL without, P = 0.009). Dogs undergoing high- rather than low-field studies were significantly more likely to have MRI abnormalities detected (82.1% vs. 52.0%, P = 0.037), and specifically were more likely to have meningeal contrast enhancement identified (48.0 vs. 12.5%, P = 0.041). Significant relationships between other clinical variables and MRI findings were not identified.

Following stepwise binary logistic regressions, dogs with spinal cord T2-W hyperintensity were found to have a significant positive association with paresis/paralysis [odds ratio (OR) 35.21; 95% confidence interval (95% CI) 1.96 to 632.46, P = 0.016] as were dogs with haemorrhage (OR 31.77; 95% CI 2.41 to 418.74, P = 0.009). No other binary logistic regressions generated significant coefficients.

Treatment

Fifty-one dogs (96.2%) received glucocorticoids. One dog underwent exploratory hemilaminectomy, revealing extradural haemorrhage, and subsequently received glucocorticoids. Fourteen dogs (26.4%) were prescribed additional immunosuppressive agents; 13 received one further (nine cytarabine, two azathioprine, one lomustine, one ciclosporin) and one received three agents (ciclosporin and cytarabine initially, with azathioprine added after 2 months due to lack of remission). One dog improved spontaneously without specific therapy (further follow-up information was unavailable).

Outcomes

Fifty-two dogs (98.1%) survived to discharge. One dog had evidence of extensive extradural/subarachnoid haemorrhage compressing the brainstem, cerebellum and cervical spinal cord, and did not receive glucocorticoids. This dog required mechanical ventilation and was euthanased due to the poor prognosis and clinical deterioration, with SRMA diagnosed via post-mortem gross examination and histopathology. Due to the high survival rate, statistical analysis regarding survival was not performed.

Of the surviving 52 dogs, follow-up data were available for 29 (55.8%). The median follow-up time was 125 days (range 12 to 2186 days). Clinical remission was recorded in all 29 dogs (100.0%), and clinical resolution in nine (31.0%). Relapse was recorded in nine dogs (31.0%), a median of 195 days (range 41 to 540 days) after starting treatment. One dog developed acute pancreatitis and pancytopenia 10 days after discharge, suspected secondary

Table 4. A summary of key MRI findings, their distribution and their severity within the study population

	Parenchymal T2-W hyperintensity	Meningeal contrast enhancement	Parenchymal contrast enhancement	Evidence of haemorrhage	Paravertebral muscle changes
Affected area					
None	38/53	28/41	34/41	48/53	23/53
Cranial	0/12	3/9	0/9	2/12	–
Cervical	10/45	11/34	5/34	3/45	22/45
Thoracic	3/13	2/7	1/7	1/13	10/13
Lumbar	3/13	1/6	0/6	1/13	8/13
Distribution					
Focal	11/15	5/13	5/6	–	6/30
Multifocal	2/15	1/13	1/6	–	24/30
Diffuse	2/15	7/13	0/6	–	0/30
Lesion severity					
Mild	6/13	3/13	2/6	–	–
Moderate	5/13	7/13	3/6	–	–
Severe	2/13	3/13	1/6	–	–

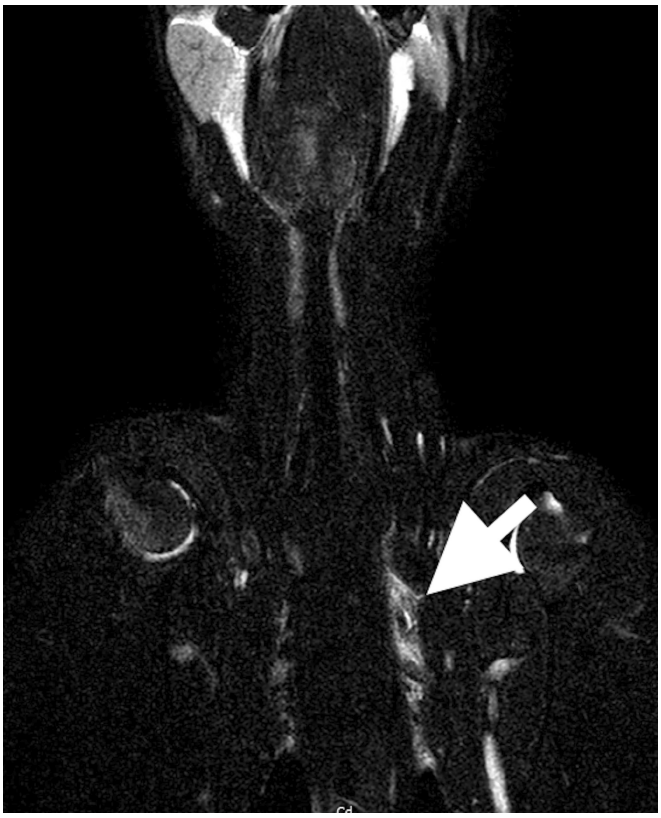

FIG 1. Dorsal T2-W fat-suppressed Dixon sequence of the caudal head, neck and cranial thorax demonstrating paravertebral muscle changes (arrow).

to azathioprine and was euthanased. No MRI findings were found to have a significant relationship with relapse occurrence.

DISCUSSION

SRMA is a key differential diagnosis for young dogs in the UK with pyrexia or spinal hyperaesthesia, with or without signs of myelopathy (Black et al., 2019; Gonçalves et al., 2022; Trevail & Behr, 2014). However, there is only scant data pertaining to MRI findings in SRMA in the UK canine population (Brocal et al., 2017). To our knowledge, this is the first case series to investigate and demonstrate the association of MRI findings with clinical variables in dogs with SRMA.

Abnormalities were identified in most studies (39/53; 73.6%), with paravertebral muscle changes most prevalent (30/53; 56.6%). Paravertebral muscle changes are not exclusive to SRMA, having been reported as a predictor of inflammatory disease generally in dogs undergoing spinal MRI (Eminaga et al., 2013). Paravertebral muscle changes have also been reported in association with intervertebral disc extrusion, therefore are not specific to inflammatory conditions alone (Morrison et al., 2021). Interestingly, there was no association between the presence of paravertebral muscle changes and the presence of increased serum CK.

When comparing to two previous SRMA case series, the total number of abnormal MRI studies was similar; 73.6% compared to the previously reported 74% and 98.6% (Lau et al., 2019; Remelli et al., 2022). Additionally, the number of cases with spinal cord parenchymal T2-W hyperintensity and spinal cord parenchymal contrast enhancement were similar; 28.3% compared to the previously reported 21.7% and 12.8% compared to 14.3%, respectively (Lau et al., 2019; Remelli et al., 2022).

Meningeal contrast enhancement was present in only 31.7% of dogs where contrast was administered, less than reported elsewhere (48% and 87.1%) for SRMA (Lau et al., 2019; Remelli et al., 2022). The reason for the difference is unclear. Case selection biases due to variations in inclusion criteria, image acquisition, image review techniques or geographical variations were potential considerations. Not all dogs with SRMA undergo MRI, with differences between institution/clinician preferences influencing this decision. This could create bias towards dogs with more severe or myelopathic presentations, who may demonstrate MRI abnormalities more frequently. However, if the population in this study had overall less severe disease compared to others, it might be expected that the prevalence of other MRI abnormalities would be lower, rather than just meningeal contrast enhancement. Additionally, the prevalence of paravertebral muscle changes was higher (56.6%) than the previously reported

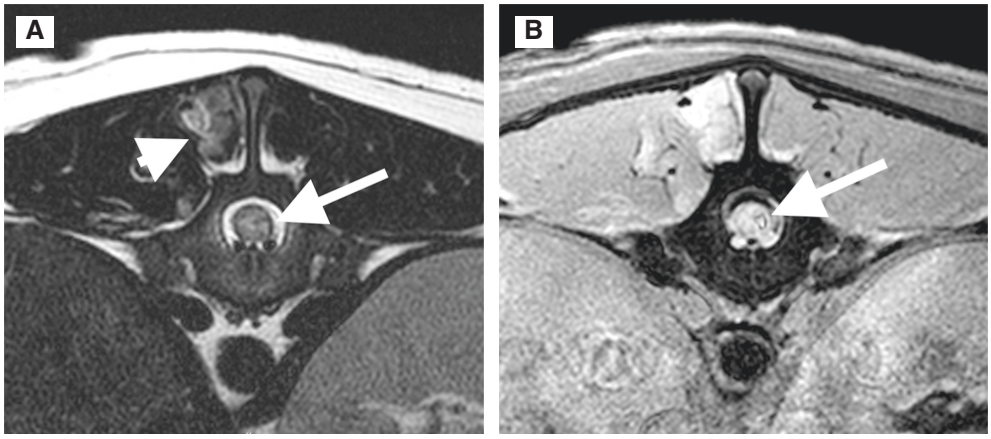

FIG 2. (A) Transverse T2-W sequence at the level of the caudal thorax showing evidence of intramedullary haemorrhage (long arrow) and paravertebral muscle changes (short arrow). (B) Transverse T2*GE sequence at the same location as (A) confirming presence of an intramedullary susceptibility artefact consistent with haemorrhage (white arrow).

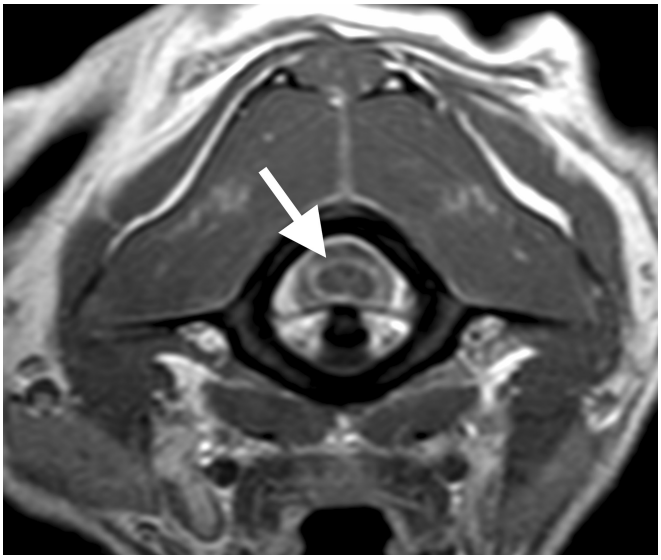

FIG 3. Transverse T1-W post-contrast image of the cervical spinal cord at the level of the atlas. There is marked meningeal contrast enhancement surrounding the spinal cord (white arrow).

26% and 48.6%, again less consistent with milder disease (Lau et al., 2019; Remelli et al., 2022).

Regarding MRI acquisition, the proportion of high-field studies (more sensitive for contrast enhancement) was higher in the current study (52.8% vs. 28.5%), meaning that lower image resolution is unlikely to account for lower meningeal contrast enhancement frequency (Remelli et al., 2022). This previous study utilised a post-processing subtraction technique to increase the detection of meningeal enhancement by a reported 10% to 15%, only partially accounting for any difference (Remelli et al., 2022). Another possible contributing factor is that in the study by Remelli et al. (2022), pre- and post-contrast T1-W series were acquired in both sagittal and transverse planes. Several patients in the current study were only examined in the sagittal plane. Consequently, subtle/focal areas of meningeal contrast enhancement could have been missed. Additionally, meningeal enhancement may be more apparent with delayed acquisition times and therefore not detected in a single T1-W series obtained immediately post-contrast (Joslyn et al., 2011).

Comparing against previous studies for discernible disparities in clinical indicators of disease severity also did not reveal stark differences. Fifteen dogs (28.3%) had myelopathic signs, comparing similarly to 10% to 47% in previous heterogenous SRMA populations (Lowrie et al., 2009; Remelli et al., 2022; Tipold & Jaggy, 1994). When comparing markers of systemic inflammation, the median neutrophil count, median CRP concentration and median body temperature were similar to previous studies, again suggesting similar disease severity (Lau et al., 2019; Lowrie et al., 2009; Remelli et al., 2022). Only a lower median CSF TNCC in the present study gave any indication that milder disease severity could be a factor (312 cells/μL compared with 735 and 945 cells/μL) (Lau et al., 2019; Remelli et al., 2022). Both previous case series included cervical spine MRI only (Lau et al., 2019; Remelli et al., 2022). In the present study, six dogs (11.3%) had a normal cervical region on MRI, with lesions identified at other locations. All six had paravertebral muscle changes, which could explain the higher prevalence of this specific MRI feature.

Regarding the initial hypothesis, we found no evidence that the presence or absence of any MRI lesions were associated with the duration of clinical signs or occurrence of remission. The effect on survival was not possible to explore, as the mortality rate was too low to allow meaningful investigation (52/53, 98.1% survival to discharge). The presence of MRI spinal cord abnormalities was associated with higher cisternal CSF TNCC and a higher paresis/paralysis incidence. Both could be considered indicators of more severe spinal cord inflammation, so it is unsurprising that observable lesions were more frequent. Similarly, paresis/paralysis had a significant positive relationship with the presence of T2-W spinal cord hyperintensity and haemorrhage. All dogs with paresis/paralysis had identifiable spinal cord parenchymal lesions or meningeal enhancement. Dogs with haemorrhage were more likely to have paresis/

paralysis (OR 31.77), as were dogs with spinal cord T2-W hyperintensity (OR 35.21). This is unsurprising particularly for haemorrhage, which can cause spinal cord compression or effacement. Previous reports have demonstrated severe haemorrhagic clinical presentations of SRMA, although its prevalence has not been explored (Brocal et al., 2017; Wang-Leandro et al., 2017; Zilli et al., 2021). Surgical management of SRMA-related haemorrhage has been described, and indeed was performed in one dog in the current study with good outcome (Zilli et al., 2021).

Haemorrhage may occur in SRMA due to rupture of vessels secondary to severe inflammation (with dissolution of arterial wall integrity) and/or thrombosis (Snyder et al., 1995; Vandevelde et al., 2012). Vasculitis associated haemorrhage has also been described in people (Lee et al., 2018; Marder et al., 2014). Other differential diagnoses to consider for haemorrhage in or around the CNS include trauma, intervertebral disc disease, neoplasia, coagulopathy and other infectious/inflammatory vascular lesions (e.g., septicaemia) (Vandevelde et al., 2012). *Angiostrongylus vasorum* infection is an important differential for CNS haemorrhage (often multifocal) in the UK. However, reported cases generally had evidence of haemorrhage/infection affecting other body systems (e.g., eyes, tongue, respiratory or urinary tract) as well as grossly haemorrhagic CSF, neither of which were present in these cases (Garosi et al., 2005; Gredal et al., 2011; Santifort et al., 2023; Wessmann et al., 2006). Hyperthermia is also very uncommon in angiostrongylosis. One dog displaying haemorrhage in the present study had post-mortem examination which was not consistent with angiostrongylosis. Two of the other four dogs affected had negative point-of-care *Angiostrongylus* antigen test, and all four dogs responded favourably to glucocorticoids without treatment for angiostrongylosis.

Nine of 29 (31.0%) dogs with follow-up relapsed, similar to 20% to 47.5% reported previously, though missing data could lead to underestimation (Biedermann et al., 2016; Hilpert et al., 2020; Lau et al., 2019; Lowrie et al., 2009; Tipold, 1995; Tipold & Jaggy, 1994). Predictors of relapse have been difficult to identify, though a younger age, higher CSF TNCC, prednisolone monotherapy and lower CRP concentrations have potentially been associated with increased risk (Biedermann et al., 2016; Hilpert et al., 2020; Lau et al., 2019). In a study investigating CT findings in dogs with SRMA, no abnormalities predicted relapse (Fuchs et al., 2000). Similarly, no MRI findings were associated with relapse in the current study. It should be emphasised however, that treatment and follow-up were not standardised and may vary based on the severity of presentation, MRI findings and clinician preference. Therefore, any conclusions regarding outcomes in a retrospective study such as this need to be considered with caution. Prospective studies, with standardised approaches, investigating predictors of outcome are warranted.

Chronic SRMA has been described, reportedly associated with relapses, variable CSF results and increased prevalence of neurological abnormalities (Tipold & Jaggy, 1994; Tipold & Stein, 2010; Trevail & Behr, 2014). However, no definitive definition of the chronic form exists to our knowledge. Including chronic and acute cases together may be suboptimal as the clinical presentation and results of investigations may differ, affecting decision making. Histological descriptions of the chronic form include lymphohistiocytic leptomeningitis, meningeal periarteritis and occasionally subdural haemorrhage or meningeal fibrosis severe enough to cause CSF obstruction (Tipold & Jaggy, 1994; Wohlsein et al., 2022). These changes may translate to attenuation of the CSF column on HASTE or other single-shot fast spin echo sequences, meningeal thickening and contrast enhancement, along with possible magnetic susceptibility artefact in cases with haemorrhage. Clinically significant haemorrhage, however, has been reported with both chronic and acute disease (Brocal et al., 2017; Hughes et al., 2015; Wang-Leandro et al., 2017; Wohlsein et al., 2022; Zilli et al., 2021). Dogs with chronic relapsing disease do not necessarily have more extensive or severe vascular lesions on histopathology, therefore more extensive changes may not be expected on MRI when compared to acute cases (Snyder et al., 1995). Certainly, there was no association in the present study between duration of clinical signs and MRI findings, and acute SRMA appeared to have potential for neurological and MRI abnormalities just as significant as chronic. Further studies with histopathological assessment alongside MRI would be necessary however to explore the different forms further.

It is reported that normothermia does not exclude SRMA, and in the current study pyrexia was recorded in only 84.9% of dogs (Lau et al., 2019; Remelli et al., 2022). Neither body temperature nor the presence of pyrexia had any significant relationship with MRI results.

One dog had normal CSF TNCC at the time of MRI acquisition, despite suggestive clinical signs. This case had been displaying clinical signs for 6 to 7 months and was included due to the demonstration of a neutrophilic pleocytosis 4 weeks later with similar clinical signs. Normal CSF findings have been reported in dogs with chronic SRMA (Remelli et al., 2022; Tipold & Jaggy, 1994).

One dog had a positive *Neospora caninum* IFAT titre of 1:200, however, displayed a negative CSF PCR, decreased titre (1:50) after 3 weeks, and an eventual clinical response to further immunosuppression rather than antibiosis. Although neosporosis was possible, previous studies have suggested titres >1:50 support exposure, and titres >1:400 to 800 or positive PCR results are consistent with active infection (Coelho et al., 2019; Didiano et al., 2020; Jones & Harcourt-Brown, 2022). Another dog had positive serological point-of-care and equivocal external laboratory *Ehrlichia canis* ELISA results (21.85 relative units, 14 to 29 units considered equivocal). Meningitis/meningoencephalitis or meningeal bleeding are uncommonly reported with ehrlichiosis, though affected dogs typically have thrombocytopenia, coagulopathy and demonstrable brain lesions (Di Dona et al., 2021; Frankar et al., 2022; Harrus et al., 2012; Harrus & Waner, 2011; Lukács et al., 2020; Mylonakis et al., 2019; Neer et al., 2002). Although clinical ehrlichiosis was not excluded without PCR or paired serology, the inconclusive titre, normal haematocrit and platelet count, acute clinical history (4 days), absence of haemorrhage and rapid positive response to glucocorticoids

were considered consistent with SRMA and incidental previous *Ehrlichia canis* exposure.

Study limitations mainly relate to the retrospective nature and those inherent to MRI review. Image acquisitions were performed as part of normal clinical practice and not standardised. Both low- and high-field systems were utilised with variable protocols, leading to variation of available sequences and imaging planes, with not all sequences available for every case. Nevertheless, all cases had a T2-W sagittal sequence of the area of interest, with almost all studies (45/53; 84.9%) including a fat suppression series (STIR or T2-W DIXON sequence), and the majority including a T1-W sequence (44/53; 83.0%) and a T1-W post-contrast administration (40/53; 75.5%). Additional findings could have been missed in areas not included. However, it may be expected that the most significant lesions would be present in the anatomical areas of interest determined by clinical examination. Limitations relating to differences in MRI acquisition and patient selection are likely more significant in a multi-centre study, where both inter-hospital and inter-clinician factors exist.

Twenty-five studies (47.2%) were acquired using a low-field MRI scanner, leading to lower spatial resolution images where less conspicuous lesions may potentially be missed. Though a recent study did not find significant differences between high- and low-field MRI capabilities in detecting abnormalities in SRMA, our study did find a higher prevalence of MRI abnormalities in the high-field studies than low-field, and of meningeal contrast enhancement specifically (Remelli et al., 2022). As the strength of the machine was directly related to the centre of origin, it could not be excluded that bias in patient selection between hospitals had an effect too. All studies were reviewed by two of the authors together, with blinded and consensus review potentially achieving higher accuracy. Still, this was a subjective process, and future work could include a scoring/grading system to help objectify data collection, as utilised elsewhere (Remelli et al., 2022).

Finally, this population and their MRI findings may not be fully representative of the global/national SRMA population. Selection bias likely exists in which dogs underwent MRI. As previously discussed, this bias and its significance may depend on the institution or clinician. The study population was selected from referral hospitals, which could reflect a more severely affected subset. Further studies, particularly prospective studies where MRI is extended to all cases, are indicated to further investigate MRI changes and their relationship with clinical variables, treatment and outcomes.

In summary, the majority of dogs in this UK study had abnormal MRI findings. Lesions can appear severe or extensive, not necessarily involving the cervical region. The most common abnormalities were paravertebral muscle changes, followed by meningeal contrast enhancement, spinal cord T2-W hyperintensity and parenchymal contrast enhancement. The presence of spinal cord MRI abnormalities, especially haemorrhage and T2-W parenchymal hyperintensity, were associated with an increased prevalence of paresis/paralysis. Identification of these lesions in dogs with appropriate signalment, presentation and clinical findings can lend further support to a diagnosis of SRMA. The authors recommend that MRI be considered for dogs that have an atypical SRMA presentation (e.g., lack of systemic inflammatory signs, older age, atypical breed), are myelopathic or have shown a poor response to appropriate therapy.

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Author contributions

B. A. Jones: Data curation (lead); formal analysis (equal); investigation (lead); methodology (supporting); project administration (lead); writing – original draft (lead); writing – review and editing (lead). **P. Agthe:** Conceptualization (equal); data curation (supporting); formal analysis (equal); investigation (supporting); methodology (supporting); supervision (supporting); writing – review and editing (supporting). **E. Scarpante:** Data curation (supporting); writing – review and editing (supporting). **A. Crawford:** Data curation (supporting); writing – review and editing (supporting). **V. Black:** Data curation (supporting); writing – review and editing (supporting). **I. Espadas:** Data curation (supporting); writing – review and editing (supporting). **S. Formoso:** Data curation (supporting); writing – review and editing (supporting). **A. R. Fraser:** Conceptualization (equal); data curation (supporting); formal analysis (equal); investigation (supporting); methodology (lead); project administration (supporting); supervision (lead); writing – original draft (supporting); writing – review and editing (supporting).

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 the paper.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

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

Table S1. Haematology results.

Table S2. Serum biochemistry results.