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CASE REPORT
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Steroid-Responsive Myelitis in Dogs - Comparison with Steroid-Responsive Meningitis-Arteritis

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ABSTRACT

***Background*:** Myelitis is the inflammation of the spinal cord parenchyma alone, whereas meningitis is the inflammation of the meninges. Steroid-responsive meningitis-arteritis (SRMA) is a meningomyelitis in which the major lesions involve the meninges, not the spinal cord parenchyma, and respond well to glucocorticoid treatment. However, myelitis in dogs has rarely been reported, and myelitis with a good response to glucocorticoid treatment without relapse has not been reported. This report describes 5 cases of steroid-responsive myelitis (SRM) in dogs.

***Cases*: *Case 1*.** A 8-year-old intact female Cocker Spaniel presented with progressive nonambulatory paraplegia. Whole spinal parenchymal lesions were identified using magnetic resonance imaging (MRI) scan. Mononuclear pleocytosis with increased total protein levels was the only abnormal finding on cerebrospinal fluid (CSF) analysis. Prednisolone (PDS) was administered followed by dose tapering according to therapeutic response. Cyclosporine was administered until the termination of PDS. Since then, no recurrence of neurological symptoms has been observed. Follow-up MRI and CSF analysis revealed resolution of previously observed abnormal findings. ***Case 2*.** A 2-year-old intact female Maltese presented with non-progressive paraparesis. A spinal parenchymal lesion in the lumbosacral region was observed on MRI. PDS was administered and slowly tapered at approximately 3-week intervals. No recurrence of neurological symptoms was observed after the treatment. ***Case 3*.** A 6-year-old intact female Miniature Pinscher presented with neck pain, along with leukocytosis and neutrophilia. Cervical spinal parenchyma lesions were revealed through MRI. Increased total protein concentration with mixed cell pleocytosis was observed on CSF analysis. Immunomodulatory therapy, similar to that in case 2, was initiated. A second MRI and CSF analysis revealed an improvement in the previously observed abnormalities. ***Case 4*.** A 2-year-old, intact female Toy Poodle presented with acute paraplegia and back pain. Lesions were observed in the spinal parenchyma at the T12-L3 levels on MRI. The treatment was conducted as in case 2. During treatment, neurological symptoms, including paraplegia and back pain, were not observed. Follow-up MRI revealed improvement in the spinal lesion. ***Case 5*.** A 6-month-old, castrated male Standard Poodle presented with progressive paraparesis. On MRI, lesions were observed in the T11-T13 regions. Immunomodulation therapy, similar to that in case 2, was initiated. No recurrence of neurological symptoms was observed after treatment initiation

***Discussion*:** SRM is similar to SRMA in terms of good steroid-responsiveness and noninfectious inflammation etiology; however, it does not exactly satisfy the diagnostic criteria for SRMA, nor does it progress similarly. The characteristics of SRM that do not satisfy the diagnostic criteria of SRMA include the absence of fever, C-reactive protein elevation, hyperglobulinemia, and relapse, and the presence of spinal parenchymal lesions without parenchymal or meningeal enhancement on MRI. It is also a seemingly different from spinal cord-only meningoencephalomyelitis of unknown origin due to its better treatment response and prognosis. However, the dogs in the present report with SRM satisfied the diagnostic criteria for transverse myelitis in human patients. Therefore, SRM, including good steroid responsiveness and good prognosis without relapse, may represent a novel type of meningomyelitis.

Keywords: canine, inflammatory spinal cord disease, myelitis, spinal cord, steroid.

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INTRODUCTION

Myelitis is defined as inflammation only in the spinal cord parenchyma, and meningitis is defined as inflammation only in meningomyelitis; however, meningomyelitis, combined with both myelitis and meningitis, mostly occurs in dogs [6,16]. Meningomyelitis is known to result from several etiologies, including infectious, immune-mediated, vascular, metabolic, or paraneoplastic causes [3].

Steroid-responsive meningitis-arteritis (SRMA) is a suspected immune-mediated spinal disorder characterized by a positive response to corticosteroids, juvenile onset (≤ 2 years old), pyrexia, neutrophilia, hyperglobulinemia, high circulating immunoglobulin A (IgA), high circulating C-reactive protein (CRP), neutrophilic pleocytosis in the cerebrospinal fluid (CSF), and meningeal contrast enhancement on magnetic resonance imaging (MRI) [11,14,15,17].

Spinal cord-only meningoencephalomyelitis of unknown origin (SMUO) is an inflammatory spinal disease with poor prognosis and low treatment responsiveness. It is clinically diagnosed based on the presence of noninfectious inflammatory myelitis that is not classified as SRMA or eosinophilic meningomyelitis [6].

Steroid-responsive myelitis (SRM) has not been reported previously. This disease responds well to immunomodulatory glucocorticoid treatment without relapse, even after the termination of treatment. The present cases demonstrate the clinical features of SRM, which could be distinguished from other inflammatory spinal cord diseases.

CASES

Case 1. A 8-year-old intact female Cocker Spaniel presented with paraplegia that had progressed over 3 weeks. Physical and neurological examinations revealed nonambulatory paraplegia, decreased proprioceptive positioning on the left thoracic limb and pelvic limbs, increased left thoracic and pelvic limb spinal reflexes, and absent extensor postural thrust (Table 1). The blood analysis results, including complete blood counts, serum chemistry, and electrolytes, were within the reference range (Table 2). The spinal parenchymal lesion on the whole spinal cord was isointense on T1-weighted images (T1W), hyperintense on T2-weighted images (T2W), and T2-fluid-attenuated inversion recovery images (FLAIR) were identified via MRI[1] (Table 3). No enhancement of the spinal parenchyma and meninges was observed. CSF analysis revealed mononuclear pleocytosis (total nucleated cell count [TNCC], 96 cells/mm^3; reference range: < 5 cells/mm^3) with increased total protein concentration (100 mg/dL; reference range: < 30 mg/dL) and 0 mg/L of CRP (reference range: <10 mg/L, Table 4) in CSF, and negative results of polymerase chain reaction (PCR) for infectious organisms (Table 5). Therefore, the dog was diagnosed with noninfectious myelitis. Prednisolone (PDS) [Solondo®[2]] was given at an initial dose of 1.5 mg/kg orally twice daily for immunosuppression, and cyclosporine [Cypol-N®[3]] was additionally administrated at dose of 5 mg/kg orally once daily. The dose of PDS was tapered according to the therapeutic response, and the final dose administered before treatment termination was 0.25 mg/kg once daily. Since the neurological symptoms improved dramatically after starting the treatment and there was no recurrence of neurological symptoms, PDS and cyclosporine were discontinued simultaneously. The total treatment duration was 131 days. Since then, no recurrence has been reported. After the termination of treatment, a second MRI was performed 194 days after the first visit to confirm the improvement of the lesions observed on MRI (Figure 1). The spinal cord parenchyma was isointense on T1W, T2W, and FLAIR images, and no contrast enhancement was observed in the spinal cord parenchyma and meninges. A second CSF analysis was conducted following the second MRI scan. The increase in total protein with pleocytosis previously identified in the first CSF analysis was improved, as total protein and TNCC were within the reference range. Therefore, it is presumed that noninfectious myelitis has a good response to steroid treatment without satisfying the criteria for SRMA.

Case 2. A 2-year-old intact female Maltese presented with non-progressive paraparesis for 2 months. Tonic muscle tone in both thoracic limbs and flaccid muscle tone in the pelvic limbs were observed. Decreased bilateral pelvic limb proprioception with absent extensor postural thrust, lower motor neuron bladder, exaggerated spinal reflexes in both pelvic limbs, hyperesthesia in the lumbosacral region, and absence of cutaneous trunci reflex were identified through physical and neurological examinations (Table 1). All parameters of blood analysis were within the reference range (Table 2). Serum CRP and Ig A were

0.3 mg/L and 37 mg/dL (reference range: 30-270 mg/dL), respectively, all within the reference range (Table 4). The spinal parenchymal lesion in the lumbosacral region was isointense on T1W, and hyperintensity on T2W and FLAIR was identified on MRI scan (Table 3). Meningeal enhancement, without spinal parenchymal enhancement, was also observed. In the CSF analysis, pleocytosis and increased total protein concentration were not confirmed (Table 5). PCR revealed no infectious organisms. Consequently, noninfectious myelitis was suspected. For immunosuppression, PDS [Solondo®2] was administered twice a day at 2 mg/kg and slowly tapered at approximately 3-week intervals. The total duration of treatment was 106 days and the final PDS dose was 0.5 mg/kg every other day. PDS was discontinued because no neurological symptoms were observed. Since no recurrence of neurological symptoms was observed during or after the treatment, the dog's disease was suspected to be a steroid-responsive form of myelitis, owing to the good response to steroid treatment without satisfying the criteria for SRMA.

***Case 3*.** A 6-year-old intact female Miniature Pinscher presented with neck pain for a day. Decreased left limb proprioception and cervical hyperesthesia were also observed. The results of the other physical and neurological examinations were normal (Table 1). Blood analyses revealed leukocytosis (19,010 × 10^3/μL; reference range: 5,050-16,760 × 10^3/μL) with neutrophilia (15,538 ×10^3/μL; reference range: 2,940-11,640 × 10^3/μL) and CRP (4.6 mg/L) within the reference range (Tables 2 & 4). The spinal parenchyma lesion was revealed through MRI scan as hyperintense on T2W and FLAIR and hypointense on T1W without contrast enhancement (Table 3). CSF analysis revealed an increased total protein concentration (30 mg/dL) with mixed cell pleocytosis (TNCC, 2,080 cells/mm^3). However, PCR revealed no infectious diseases in the dogs (Table 5). Therefore, the dog was presumptively diagnosed with noninfectious myelitis, and immunomodulatory therapy was initiated. Immunomodulatory therapy was scheduled as follows: PDS [Solondo®2] administration was started at 2 mg/kg twice a day and was reduced by 25% every 3 weeks. The second MRI scan was performed 183 days after the start of myelitis treatment. The lesion identified on the first MRI scan was isointense on FLAIR and T1W images (Figure 1). After the second MRI scan, CSF analysis was performed. Total protein, previously observed to be increased, was within the reference range, and mixed cell pleocytosis changed to lymphocytic pleocytosis. TNCC decreased from 2,080 cells/mm^3 to 200 cells/mm^3 confirming that there was a comprehensive therapeutic response. Therefore, tapering of the PDS was maintained. The dose immediately before the termination of the treatment was 0.5 mg/kg every other day. Even after PDS tapering, no recurrence of neurological symptoms was observed, and all medications were discontinued. The total treatment duration was 264 days. Therefore, this dog was suspected of having had a steroid-responsive form of myelitis, owing to the good response to steroid treatment without satisfying the criteria for SRMA.

***Case 4*.** A 2-year-old intact female Toy Poodle presented with acute paraplegia and back pain for one day. Absent bilateral pelvic limb proprioception, spinal hyperesthesia in the thoracolumbar region, and exaggerated spinal reflexes in the bilateral pelvic limbs were identified on neurological examination. The cutaneous trunci reflex was consistently absent at the level of L1 to L2 on both sides (Table 1). Only hyperalbuminemia (4.6 g/dL; reference range: 2.6-3.3 g/dL) and hypoglobulinemia (1.8 g/dL; reference range: 2.7 - 4.4 g/dL) were found to be abnormal in blood analyses. Serum CRP (0 mg/L) and IgA (60 mg/L) levels were all within the reference ranges (Tables 2 and 4). MRI scans were conducted in the thoracolumbar region, and lesions were observed in the spinal parenchyma at the T12-L3 level (Table 3). The lesion was hyperintense on T2W and FLAIR, isointense on T1W, and without enhancement of the parenchyma and meninges. The total protein concentration (< 30 mg/dL) was within the reference range and pleocytosis was not observed in the CSF. Infectious organisms were also not detected by the PCR analysis (Table 5). The dog was finally diagnosed with presumptive noninfectious myelitis. Glucocorticoide-based immunomodulatory therapy was initiated to treat myelitis. Treatment was initiated with 2 mg/kg twice a day of PDS [Solondo®2], and the dose of PDS was tapered at approximately 3 weeks intervals. The final dose of PDS was 0.5 mg/kg every third day. The total duration of PDS administration was 246 d. During treatment, neurological symptoms, including paraplegia and back pain, were not observed. At the end of the treatment period, a second MRI scan was conducted. The T12 to L3 level lesion observed in the first MRI scan were revealed by the second MRI as follows: hyperintense on T2W, isointense on T1W

and FLAIR, and no contrast-enhanced lesion (Figure 1). MRI revealed that the lesion had improved with no neurological symptoms; therefore, medication was discontinued and treatment was terminated. Therefore, it was determined that this dog had a steroid-responsive form of myelitis, owing to the good response to steroid treatment without satisfying the criteria for SRMA.

***Case 5*.** A 6-month-old castrated male Standard Poodle presented with progressive paraparesis for six days. Decreased bilateral pelvic limb proprioception was the only abnormal finding on physical and neurological examination (Table 1). Results of blood analyses parameters including white blood cell counts (WBC, 15,070 $\times 10^3/\mu L$), neutrophil counts (8,800 $\times 10^3/\mu L$), albumin (3.2 g/dL), globulin (2.8 g/dL) and CRP (0.3 mg/L) were within reference range (Tables 2 & 4). MRI revealed T1W hypointense and T2W hyperintense lesions in the T11-T13 regions (Table 3). Contrast enhancement and FLAIR sequences were not performed because of the difficulty in maintaining anesthesia. CSF analysis revealed no pleocytosis (< 30 mg/dL), and an increased total protein concentration (TNCC, 0 cells/mm^3) was not observed (Table 5). Infectious organisms were also not detected via PCR. Noninfectious myelitis was suspected based on the test results. PDS [Solondo®[2]] was initially administered at 2 mg/kg orally twice daily for immunosuppression, and the dose was tapered according to the therapeutic response. The final PDS dose of before treatment termination was 0.5 mg/kg once daily. The total treatment duration was 83 days. No recurrence of the neurological symptoms was observed after treatment initiation. Thus, the dog was diagnosed with steroid-responsive myelitis, owing to the good response to steroid treatment without satisfying the criteria for SRMA.

DISCUSSION

The most common noninfectious inflammatory canine spinal disease is SRMA, whereas myelitis alone is rare in dogs. In canine meningomyelitis, meningomyelitis of unknown origin and granulomatous meningomyelitis are the most common diagnoses [11], whereas noninfectious myelitis with glucocorticoid responsiveness has not been well-described in dogs. The only previous report of SMUO suggested that its prognosis and long-term survival are poor [6]. In the present study, the clinical and diagnostic features of five dogs with SRM that differed from those of previously reported types of myelitis are described.

SRMA can also occur in any breed or sex. Its age of predisposition is 3 months to 9 years [13]. In contrast, the reported median age of onset of SMUO is approximately 56 months, and males are predisposed to SMUO [6]. The 5 dogs with SRM in the present study included small and large breeds, with no apparent

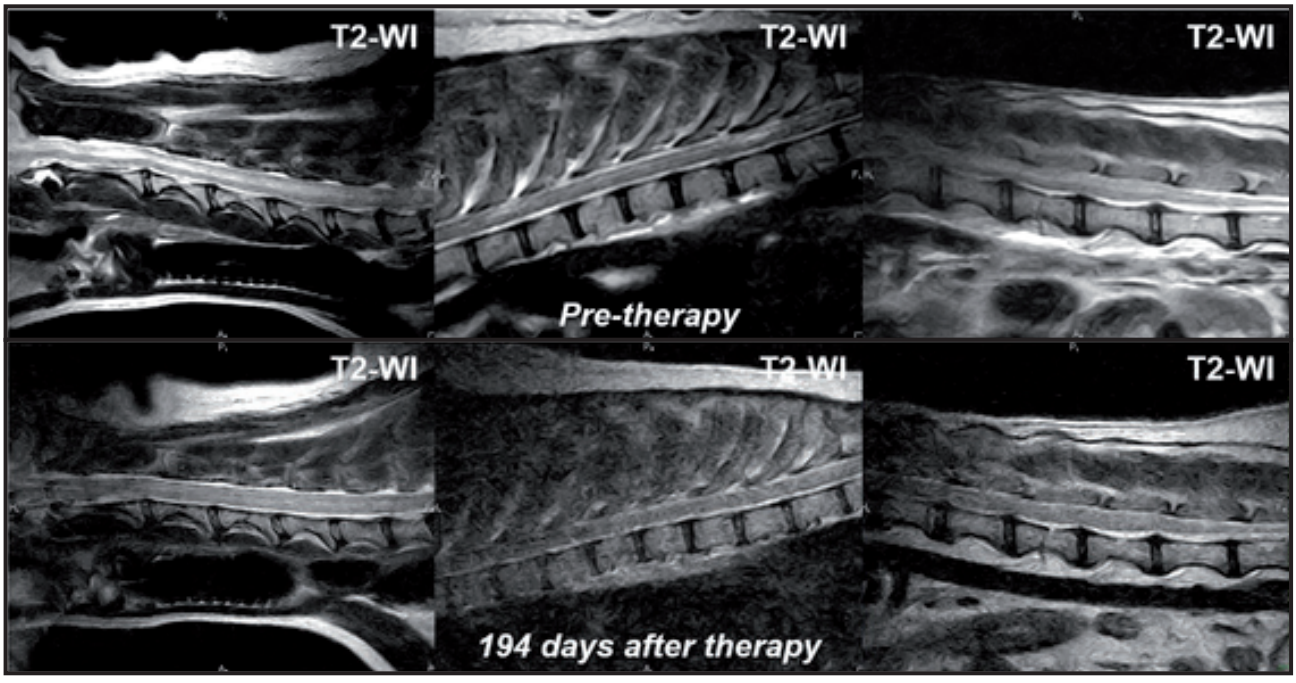

Figure 1. Changes on magnetic resonance (MR) images in dog (case 1) with steroid-responsive myelitis during steroid therapy. T2-weighted images (T2-WI) and T2-fluid-attenuated inversion recovery images (FLAIR) showed hyperintense lesions of the spinal parenchyma at the cervical, thoracolumbar and lumbosacral levels. Spinal lesions were not present on T2-WI 194 days after the initiation of steroid therapy.

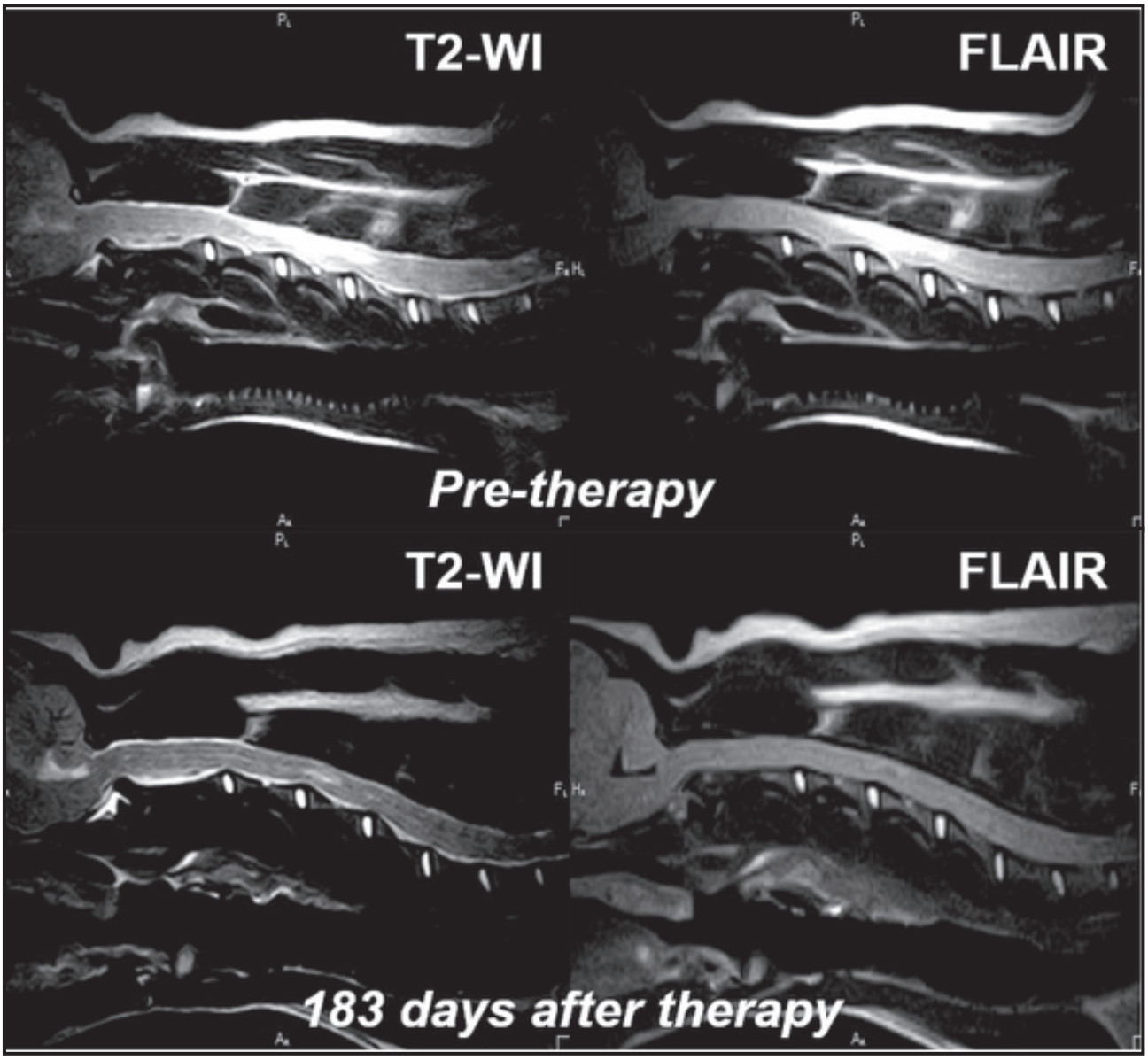

Figure 2. Changes on magnetic resonance (MR) images in dog (case 3) with steroid-responsive myelitis during steroid therapy. T2-weighted images (T2-WI) and T2-fluid-attenuated inversion recovery images (FLAIR) showed hyperintense lesions of the spinal parenchyma at the C3-C5 region. Reductions of the previous spinal lesions 183 days after the initiation of steroid treatment.

predilection for age or breed. However, these dogs comprised 4 intact bitches and 1 castrated male, which may suggest a relationship between sex hormones and SRM. Consistent with this result, there is a higher prevalence of multiple sclerosis and neuromyelitis optica in women than that in men, which may indicate a relationship between sex hormones and immune-mediated neurologic diseases [1,18]. Although a generalizable conclusion cannot be drawn due to the small number of cases, SRM appeared to have a different sex predisposition to SRMA and SMUO, and was suspected to have a pathophysiology similar to that of multiple sclerosis and optic neuromyelitis in humans.

Dogs with SRMA most commonly present with generalized ataxia, tetraparesis, paraparesis, cervical rigidity, pain, and fever [5]. In dogs with SRM, neurologic symptoms similar to SRMA were identified; however, fever was absent. Therefore, the presence or absence of fever may be the main distinguishing factor between SRM and SRMA.

On MRI, all 5 dogs with SRM showed hyperintensity on T2W and FLAIR and hypointensity or isointensity on T1W at various sites: cervical, thoracic, lumbar, and whole spinal parenchyma. Except for case 2, neither the meninges of the spinal cords nor the spinal parenchyma showed contrast enhancement.

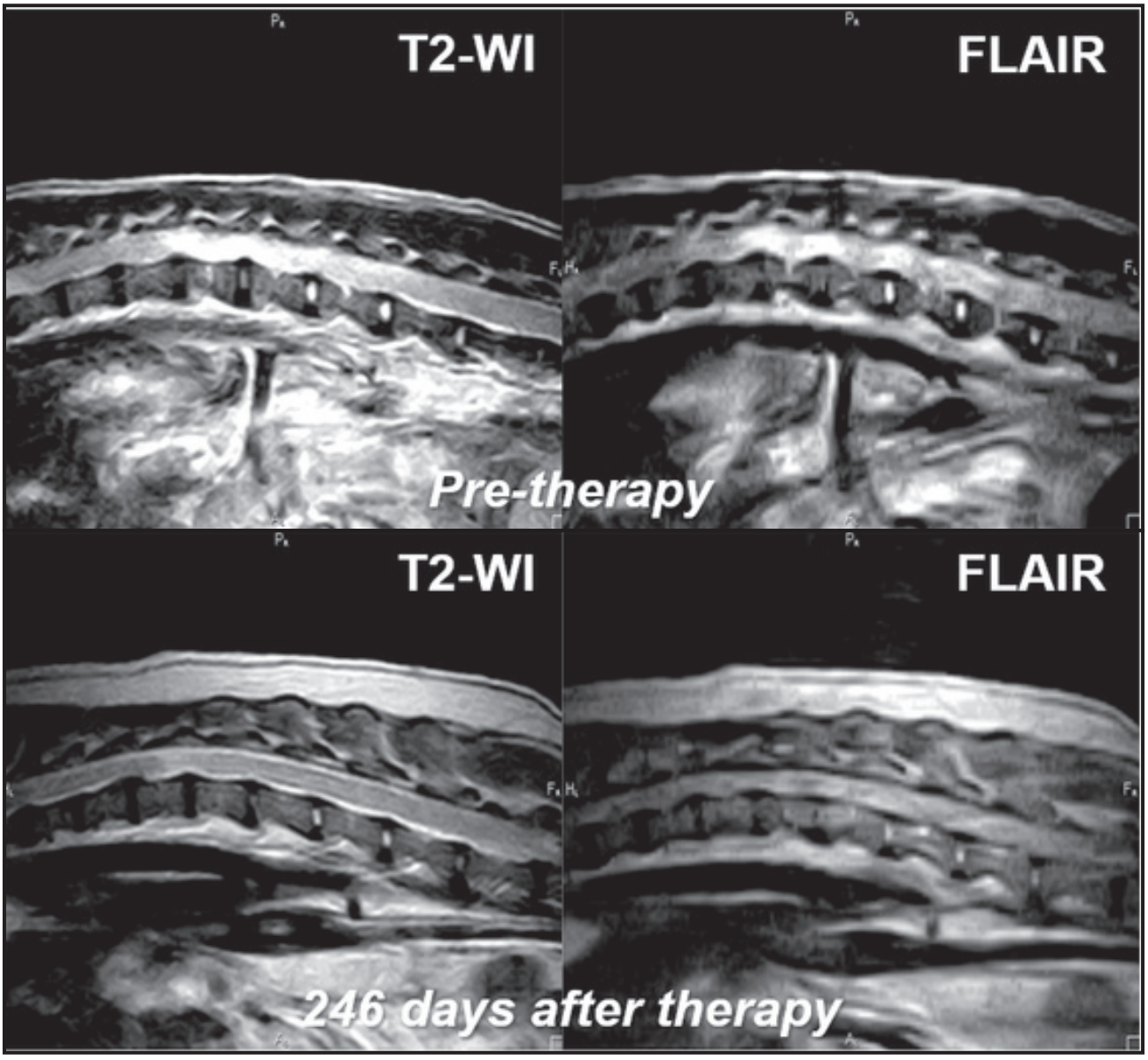

Figure 3. Changes on magnetic resonance (MR) images in dog (case 4) with steroid-responsive myelitis during steroid therapy. T2-weighted images (T2-WI) and T2-fluid-attenuated inversion recovery images (FLAIR) showed hyperintense lesions of the spinal parenchyma at the T12-L3 region. MR images demonstrated reductions in the spinal lesions 246 days after the initiation of steroid treatment.

Meningeal enhancement is characteristic in MRI of dogs with SRMA, and contrast enhancement of overlying meninges was reported in 81% of lesions in dogs with SMUO [6,15]. Furthermore, spinal parenchymal contrast enhancement was reported in 86% of lesions in dogs with SMUO. In SRMA and SMUO, contrast enhancement in the meninges, spinal parenchyma, or both was identified at a high rate, whereas in SRM in the present study, contrast enhancement in the spinal parenchyma and meninges was identified at a relatively low rate. Therefore, the absence of contrast enhancement in the lesion may be a characteristic of SRM.

Clinicopathological characteristics of SRMA include neutrophilic leukocytosis, hyperglobulinemia, and elevated IgA and CRP concentrations [15]. Neutrophilic leukocytosis was observed in only 1 dog with SRM (case 3), and none of the dogs with SRM had elevated serum or CSF CRP or IgA levels. SRMA can be induced by infectious agents and is maintained by defects in the immune system [12,15]. In dogs with SRM, hyperglobulinemia and elevated CRP and IgA levels, which indicate inflammation or infection, were not observed; therefore, the etiology of SRM may be different from that of SRMA, including infection could be carefully suggested.

Table 1. Signalment and neurologic abnormalities of the 5 dogs with steroid-responsive myelitis.

	Signalment	Neurological abnormalities	Duration of steroid therapy
Case 1	Cocker Spaniel 8-year-old Intact female 39ºC	Nonambulatory paraplegia Decreased proprioceptive positioning on left side limbs Increased left side limbs spinal reflexes Absent extensor postural thrust	131 days
Case 2	Maltese 2-year-old Intact female 39.1ºC	Paraparesis Tonic muscle tone in bilateral thoracic limbs Flaccid muscle tone in pelvic limbs Decreased pelvic limbs proprioception Absent extensor postural thrust Lower motor neuron bladder Exaggerated spinal reflexes in pelvic limbs Hyperesthesia in lumbosacral region Absent cutaneous trunci reflex	106 days
Case 3	Miniature Pinscher 6-year-old Intact female 38.2ºC	Cervical hyperaesthesia Decreased left side limbs proprioception	264 days
Case 4	Toy Poodle 2-year-old Intact female 38.6ºC	Paraplegia Thoracolumbar hyperaesthesia Absent pelvic limbs proprioception Exaggerated spinal reflexes of pelvic limbs Cutaneous trunci reflex was constantly absent at the level of L1 to L2 both side region	246 days
Case 5	Standard Poodle 6-month-old Castrated male 39.4ºC	Paraparesis Decreased pelvic limbs proprioception	83 days

Table 2. White blood cell counts and serum protein concentrations in the 5 dogs with steroid-responsive myelitis.

	WBC	Neutrophil count	Albumin (g/dL)	Globulin (g/dL)
Case 1	6,850	5,802	2.6	3.5
Case 2	8,450	6,515	2.8	2.6
Case 3	19,010	15,588	2.9	3.1
Case 4	14,170	11,830	4.6	1.8
Case 5	15,070	8,800	3.2	2.8
Reference range	5,050-16,760	2,940-11,640	2.6-3.3	2.7-4.4

WBC: white blood cell count.

Acute SRMA is characterized by neutrophilic pleocytosis in the CSF [15]. However, results of CSF analysis in dogs with SRM, 2 dogs (cases 1 & 3) demonstrated pleocytosis with elevated total protein concentration, which were identified as a mononuclear pleocytosis and a mixed cell pleocytosis at the initial visit. Furthermore, after immunomodulatory glucocorticoid treatment, the elevated total protein concentration in the CSF of both dogs decreased to within the reference range.

Table 3. Magnetic resonance imaging findings of the 5 dogs with steroid-responsive myelitis.

		Case 1	Case 2	Case 3	Case 4	Case 5
Spinal lesion						
Area		Parenchyma	Parenchyma	Parenchyma	Parenchyma	Parenchyma
Spinal segments		Whole spine	Lumbosacrum	C3-C5	T12-L3	T11-13
MR sequences						
1st scan	T1W	Isointense	Isointense	Hypointense	Isointense	Isointense
	T2W	Hyperintense	Hyperintense	Hyperintense	Hyperintense	Hyperintense
	FLAIR	Hyperintense	Hyperintense	Hyperintense	Hyperintense	NA
	T1W-CE	None	Meninges	None	None	NA
2nd scan	T1W	Isointense	NA	Isointense	Isointense	NA
	T2W	Isointense	NA	Hyperintense	Hyperintense	NA
	FLAIR	Isointense	NA	Isointense	Isointense	NA
	T1W-CE	None	NA	None	None	NA
Time between the 1st and 2nd scans		194 days		183 days	246 days	

T1W: T1-weighted images. T2W: T2-weighted images. FLAIR: T2-fluid-attenuated inversion recovery T1W-CE: T1-weighted contrast-enhanced image. NA: not assessed. MR: magnetic resonance.

Table 4. C-reactive protein and immunoglobulin A concentrations in the serum and cerebrospinal fluid of the 5 dogs with steroid-responsive myelitis.

	Sample	Case 1	Case 2	Case 3	Case 4	Case 5	Reference range
CRP (mg/L)	Serum	NA	0.3	4.6	0	0.3	0-10
	CSF	0	NA	0.3	NA	NA	
Ig A (mg/dL)	Serum	NA	37	NA	60	NA	35-270
	CSF	NA	NA	NA	NA	NA	

CRP: C-reactive protein. Ig A: immunoglobulin A; CSF: cerebrospinal fluid. NA: not assessed.

The relapse of SRMA is common even after treatment, occurring in up to one-third of dogs with SRMA [4]. In addition, in dogs with granulomatous meningoencephalomyelitis or necrotizing meningoencephalomyelitis, recurrence after discontinuation of glucocorticoids has been reported [8-10]. However, in the present study's dogs with SRM, relapse did not occur even after glucocorticoid treatment. These differences, such as good glucocorticoid responsiveness and good prognosis without relapse, are the most obvious differences between SRM and SRMA or SRMA.

Acute transverse myelitis is an acquired immune-mediated spinal cord disease in humans that can present with a rapid onset of neurologic dysfunction and is typically monophasic [2]. Transverse myelitis can occur after vaccination as an infectious disease, or alongside multiple sclerosis, neuromyelitis optica, or paraneoplastic syndrome; if the cause cannot be identified, it is termed as idiopathic transverse myelitis [19]. Diagnostic criteria have been developed for idiopathic transverse myelitis, but the presence of all criteria is not required for idiopathic transverse myelitis to be diagnosed.

The diagnostic criteria were as follows:

1. sensory, motor, or autonomic dysfunction attributable to a spinal cord lesion;
2. a T2W-hyperintense signal on spinal MRI;
3. no evidence of a compressive cord lesion;
4. bilaterality of neurological signs and/or symptoms;
5. inflammation characterized by CSF pleocytosis, high immunoglobulin G index, or gadolinium enhancement on MRI; and
6. progression to nadir within 4-21 days [20].

Table 5. Cerebrospinal fluid analysis results of the 5 dogs with steroid-responsive myelitis before and after steroid therapy.

		Case 1	Case 2	Case 3	Case 4	Case 5	Reference Range
1st Exam	TP (mg/dL)	100	<30	30	<30	<30	<30
	TNCC (cells/mm3)	96	0	2,080	0	0	<5
	Pleocytosis	Mononuclear	NO	Mixed cell	NO	NO	
	PCR	Negative	Negative	Negative	Negative	Negative	
2nd Exam	TP (mg/dL)	<30	NA	<30	NA	NA	<30
	TNCC (cells/mm3)	1	NA	200	NA	NA	<5
	Pleocytosis	NO	NA	Lymphocytic	NA	NA	
	PCR	NA	NA	NA	NA	NA	
Time between 1st and 2nd exam		194 days		183 days			

TP: total protein. TNCC: total nucleated cell count. PCR: polymerase chain reaction. NO: not observed. NA: not assessed.

When these diagnostic criteria for transverse myelitis were applied to dogs with SRM in the present study, the characteristics of the disease were consistent with those of transverse myelitis. Since neurological dysfunction in dogs with SRM did not relapse, SRM appears to differ from the recognized inflammatory spinal cord diseases in dogs, including SRMA and SMUO, and SRM may be more similar to transverse myelitis. Most human patients with idiopathic transverse myelitis usually recover within 1-3 months [7], which is consistent with the clinical course of dogs with SRM; in particular, the rapid improvement in neurological signs without relapse following an immunomodulatory dose of glucocorticoid was different from previously reported diseases involving canine meningomyelitis, including SRMA and SMUO.

The present study had several limitations. First, because the number of included dogs was small, only limited characterization of SRM was possible. Therefore, further studies with larger numbers of dogs with suspected SRM are required. Second, although the 5 dogs had characteristics that satisfied the diagnostic criteria for transverse myelitis in humans, other diagnostic tests for transverse myelitis, including the assessment of the oligoclonal band in the CSF, were not performed. Therefore, the relationship we identified between SRM and transverse myelitis should be applied with caution [2]. Third, because all dogs survived, histopathological analyses were not performed.

In conclusion, SRM, a good steroid-responsive myelitis without relapse, may be a novel inflammatory spinal cord disease that differs from that previously reported in canine meningomyelitis, including SRMA and SMUO.

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Declaration of interest. The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of this manuscript.

REFERENCES

1 **Avila M., Bansal A., Culberson J. & Peiris A.N. 2018.** The role of sex hormones in multiple sclerosis. *European Neurology*. 80(1-2): 93-99.

2 **Awad A. & Stüve O. 2011.** Idiopathic transverse myelitis and neuromyelitis optica: clinical profiles, pathophysiology and therapeutic choices. *Current Neuropharmacology*. 9(3): 417-428.

3 **Besteiro B. & Guimarães J. 2017.** Review of the etiological causes and diagnosis of myelitis and its medical orientation protocol. *Journal of Neurology and Neurophysiology*. 8: 415. DOI: 10.4172/2155-9562.1000415

4 **Biedermann E., Tipold A. & Flegel T. 2016.** Relapses in dogs with steroid-responsive meningitis-arteritis. *The Journal of Small Animal Practice*. 57(2): 91-95.

5 **Cizinauskas S., Jaggy A. & Tipold A. 2000.** Long-term treatment of dogs with steroid-responsive meningitis-arteritis: clinical, laboratory and therapeutic results. *The Journal of Small Animal Practice*. 41(7): 295-301.

6 **Cornelis I., Volk H.A., Van Ham L. & De Decker S. 2017.** Clinical presentation, diagnostic findings and outcome in dogs diagnosed with presumptive spinal-only meningoencephalomyelitis of unknown origin. *The Journal of Small Animal Practice*. 58(3): 174-182.

7 **Defresne P., Hollenberg H., Husson B., Tabarki B., Landrieu P., Huault G., Tardieu M. & Sébire G. 2003.** Acute transverse myelitis in children: clinical course and prognostic factors. *Journal of Child Neurology*. 18(6): 401-406.

8 **Dewey C.W. 2016.** Encephalopathies: Disorders of the Brain. In: *Practical Guide to Canine and Feline Neurology*. Hoboken: John Wiley & Sons, pp.141-236.

9 **Jung D.I., Kang B.T., Park C., Yoo J.H., Gu S.H., Jeon H.W., Kim J.W., Heo R.Y., Sung H.J., Eom K.D., Lee J.H., Woo E.J. & Park H.M. 2007.** A comparison of combination therapy (cyclosporine plus prednisolone) with sole prednisolone therapy in 7 dogs with necrotizing meningoencephalitis. *The Journal of Veterinary Medical Science*. 69(12): 1303-1306.

10 **Jung D.I., Kim J.W. & Park H.M. 2012.** Long-term immunosuppressive therapy with cyclosporine plus prednisolone for necrotizing meningoencephalitis in a Pekingese dog. *The Journal of Veterinary Medical Science*. 74(6): 765-769.

11 **Lowrie M., Smith P.M. & Garosi L. 2013.** Meningoencephalitis of unknown origin: investigation of prognostic factors and outcome using a standard treatment protocol. *The Veterinary Record*. 172(20): 527. DOI: 10.1136/vr.101431

12 **Maiolini A., Carlson R. & Tipold A. 2012.** Toll-like receptors 4 and 9 are responsible for the maintenance of the inflammatory reaction in canine steroid-responsive meningitis-arteritis, a large animal model for neutrophilic meningitis. *Journal of Neuroinflammation*. 9: 226. DOI: 10.1186/1742-2094-9-226

13 **Rose J.H., Kwiatkowska M., Henderson E.R., Granger N., Murray J.K. & Harcourt-Brown T.R. 2014.** The impact of demographic, social, and environmental factors on the development of steroid-responsive meningitis-arteritis (SRMA) in the United Kingdom. *Journal of Veterinary Internal Medicine*. 28(4): 1199-1202.

14 **Schwartz M., Puff C., Stein V.M., Baumgärtner W. & Tipold A. 2011.** Pathogenetic factors for excessive IgA production: Th2-dominated immune response in canine steroid-responsive meningitis-arteritis. *Veterinary Journal*. 187(2): 260-266.

15 **Tipold A. & Schatzberg S.J. 2010.** An update on steroid responsive meningitis-arteritis. *The Journal of Small Animal Practice*. 51(3): 150-154.

16 **Tipold A. & Stein V.M. 2010.** Inflammatory diseases of the spine in small animals. *The Veterinary Clinics of North America Small Animal practice*. 40(5): 871-879.

17 **Tipold A., Vandevelde M. & Zurbriggen A. 1995.** Neuroimmunological studies in steroid-responsive meningitis-arteritis in dogs. *Research in Veterinary science*. 58(2): 103-108.

18 **Wingerchuk D.M. 2009.** Neuromyelitis optica: effect of gender. *Journal of the neurological Sciences*. 286(1-2): 18-23.

19 **West T.W., Hess C. & Cree B.A. 2012.** Acute transverse myelitis: demyelinating, inflammatory, and infectious myelopathies. *Seminars in Neurology*. 32(2): 97-113.

20 **Yiu E.M., Kornberg A.J., Ryan M.M., Coleman L.T. & Mackay M.T. 2009.** Acute transverse myelitis and acute disseminated encephalomyelitis in childhood: spectrum or separate entities? *Journal of Child Neurology*. 24(3): 287-296.