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C-reactive protein in dogs with suspected bacterial diskospondylitis: 16 cases (2010–2019)

George Nye ,[1] Francois-Xavier Liebel ,[2] Tom Harcourt-Brown[2]

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[1]School of Veterinary Sciences, University of Bristol Faculty of Medical and Veterinary Sciences, Bristol, UK
[2]Neurology, Langford Veterinary Services, Langford, UK

Correspondence to
Dr George Nye; gn17257@bristol.ac.uk

ABSTRACT

Objectives C-reactive protein (CRP) is an acute phase protein used in multiple canine inflammatory conditions including steroid responsive meningitis-arteritis, immune-mediated polyarthritis and bronchopneumonia. The aim of this study was to assess whether serum CRP is elevated in cases of diskospondylitis.

Methods Medical records from 2010 to 2019 were searched to identify dogs diagnosed with diskospondylitis based on findings consistent on CT or MRI and with CRP tested.

Results A total of 16 dogs met the inclusion criteria. All cases had back pain. Fourteen cases had elevated CRP, with a median value of 100.7 mg/l (reference range for CRP values: 0–10 mg/l), 12 were pyrexic and six had leucocytosis. The two dogs with normal CRP were normothermic and did not have leucocytosis. CRP was measured four to six weeks into antimicrobial treatment in eight of 14 dogs and was normal in all cases. One dog developed a suspected bacterial empyema diagnosed on MRI; this occurred two weeks after antibiotic treatment was discontinued based on a normal CRP level at follow-up.

Conclusions Serum CRP is elevated in cases of diskospondylitis and may be clinically more useful to screen dogs with back pain than pyrexia or leucocytosis alone. Further long-term clinical evaluation in a prospective study is needed to assess its use as a treatment monitoring tool and in decision making.

INTRODUCTION

Diskospondylitis is infection of the intervertebral disc and the adjacent endplates of the vertebral bodies, most commonly bacterial,[1–6] but can also be associated with fungal disease,[7] that reaches the site most commonly by haematogenous spread, but can also be via migrating foreign body, penetrating wound or surgery.[8] The dense capillary bed of the vertebral endplate[8 9] is the hypothesised site for septic emboli to lodge and facilitate infection, with the urinary tract, skin and heart considered the most likely primary sites of infection.[8] Back pain is the most common reported clinical sign of diskospondylitis in dogs.[8] Differentiation from other potentially self-limiting causes of back pain (eg, intervertebral disc herniation) can be difficult based on clinical examination alone as only 30 per cent of diskospondylitis cases have been reported to have a systemic sign of disease, for example, leucocytosis, weight loss or pyrexia.[8 10] Diskospondylitis can be hard to treat often with long courses (ranging from six weeks to several months) of antimicrobials[2 8 11]; however, there are no published reports to critically evaluate this. A rapid diagnostic test that could raise suspicion of diskospondylitis, where a conservative approach may have been preferred or be used as a guide to successful antimicrobial treatment, would be useful to aid investigation or management of diskospondylitis.

Serum C-reactive protein (CRP) is an acute phase protein that is used as an ancillary diagnostic test in multiple canine inflammatory disorders including steroid responsive meningitis-arteritis (SRMA),[12 13] inflammatory bowel disease[14] and immune-mediated polyarthritis (IMPA),[15] as well as neoplastic (haemangiosarcoma) and infectious diseases (pyometra).[16] It has been used as a monitoring tool when using long-term courses of immunosuppressive medication[17] or potentially as a marker for predicting disease relapse.[18] Only mild elevations of serum CRP have been reported in intervertebral disc disease.[12 19]

The primary aim of this study was to investigate whether CRP is elevated in canine diskospondylitis by retrospectively reviewing cases where CRP had been measured in affected dogs, with the hypothesis that CRP is elevated in cases of diskospondylitis. The secondary aims were to compare the proportion of cases with elevated CRP with other clinical signs and clinical pathology findings, and to assess if one clinical sign or diagnostic finding was present in all cases. Finally, the authors wanted to assess what happened to CRP values following antibiotic treatment, when available.

MATERIALS AND METHODS

Study design

This was a retrospective, descriptive, single-centre case series performed at a university referral hospital in the UK between 2010 and 2019. All patients were client-owned dogs. Paper copy and electronic medical records were reviewed to identify dogs presenting with apparent back pain that had a diagnosis of diskospondylitis. The keywords for electronic records searches were 'discospondylitis' or 'diskospondylitis'. Diagnosis was based on compatible clinical signs and suggestive diagnostic imaging findings from previously published criteria,[20–22] including loss of endplate margin definition and lysis of the vertebrae adjacent to the disc space[20] on plain radiographs; T2-weighted and short tau inversion recovery (STIR) hyperintense intervertebral discs, T1-weighted hypointense and STIR hyperintense endplates[22] on MRI; and osteolysis of the adjacent vertebral endplates with or without concurrent osteolysis of the underlying bone[21] on CT.

Inclusion and exclusion criteria

Dogs were included in the study if there was a complete medical record, diagnostic imaging findings were compatible with diskospondylitis on CT or MRI, and CRP had been measured at the time of diagnosis. Presence of pyrexia, weight loss or leucocytosis at presentation were obtained from medical notes, as well as CRP values at initial sampling (and subsequent samples when performed) and bacteriology results (urine, blood or disc aspirate). Dogs were excluded if there were incomplete medical records, diagnostic imaging was not compatible with diskospondylitis, or CRP had not been measured.

Medical records review

Data collected included breed, age, bodyweight, clinical signs, presence of pyrexia (rectal temperature >39.5°C), serum CRP, haematology, biochemistry, CRP value, imaging modality (radiographs, CT, MRI), urine, blood and/or disc culture and sensitivity results, prior medications, and where applicable a post-treatment follow-up CRP, follow-up time and response to treatment. Any comorbidities were also documented. Aseptic cystocentesis was performed for culture of urine. Routine procedure for blood culture was aseptic, with three separate sites for venepuncture, requiring 10 ml of blood, each 1 hour apart before antibiotic therapy for aerobic and anaerobic and when requested fungal culture.

Statistical analysis

Descriptive data are reported as median values (minimum to maximum values) obtained using a commercially available spreadsheet software (Excel, Microsoft Office 16, Redmond, Washington).

RESULTS

Thirty dogs with a diagnosis of diskospondylitis based on various imaging modalities were identified. Twenty-six cases had either MRI or CT or both; four cases were based on radiographs only. Fourteen of these dogs were excluded because no CRP had been tested (12 dogs) or diagnosis was based on radiographs only (two dogs). Sixteen dogs were included for further data collection.

The most represented breeds were Labrador retriever (n=3), English bulldog (2) and French bulldog (2). Other breeds included flat-coated retriever, Cavalier King Charles spaniel, springer spaniel, border terrier, Irish wolfhound, whippet and German shepherd dog. There were two mixed-breed dogs. Of the 16 dogs, six were females (two spayed and four entire) and 10 were males (six neutered and four entire). The median age of all dogs was 48 months (9–152 months) and the median weight was 22.9 kg (6.5–92 kg).

All 16 dogs had back pain. Other clinical signs reported included lethargy (8), ambulatory paraparesis/tetraparesis (5), lameness (2), weight loss (2), diarrhoea (2), vomiting (1), dysuria (1) and pollakiuria (1). Pyrexia at the time of presentation was identified in 12 cases (table 1). Other comorbidities were bilateral otitis externa (case 5), perianal adenoma (case 6), IMPA (case 10) and urinary tract obstruction (case 12). A primary infection site was identified in two cases: a scrotal abscess (case 5) and a sublumbar tracking foreign body (case 13).

MRI was performed in nine dogs (figure 1), CT was performed in nine dogs (see figure 2), and radiographs were performed in four dogs (table 2). Two forms of modality were used for six dogs (three dogs had CT and radiographs, two dogs underwent CT and MRI, and one dog had both MRI and radiographs). Multiple discs were affected in three of 16 cases; suspected sternebrae infection was also evident on CT in cases 12 and 16.

Serum CRP was elevated in 14 of 16 dogs, with a median value of 100.7 mg/l (range, 3.4–240 mg/l; reference range, 0–10 mg/l) (figure 3). The CRP value was greater than 100 mg/l in eight of 16 cases. Both cases with normal CRP had no haematological changes and one had negative blood, urine and disc cultures despite surgical aspirates of a grossly affected disc (this case had received antibiotic therapy before the surgical aspirates). Haematological changes were present in eight of 16 cases, with neutrophilia (n=6), normal cell count but toxicity evident (1) and occasional reactive lymphocytes (1) reported (figure 4). Antimicrobials were started before CRP measurement in seven of 16 cases, and CRP was elevated in five of seven cases. CRP was measured in eight of 14 cases four to six weeks into starting empirical or sensitivity-based antimicrobials. All eight cases had a normal CRP value. Of these eight cases, one presented for re-examination due to a relapse of clinical signs and was subsequently euthanased due to an MRI-documented recurrence of diskospondylitis with epidural empyema and pain (figure 5).

Blood culture was performed in 15 cases, urine culture was performed in 16 cases, and disc aspirates were performed in nine cases (table 3). Four disc aspirates were fluoroscopy-guided, three were CT-guided, and

Table 1 Signalment, clinical signs and examination, and neuroanatomical localisation of each case

Case	Signalment	History	Clinical examination	Neurological localisation
1	2-year-old FE French bulldog	Acute-onset vocalisation	Lumbar back pain, weight loss, decreased pelvic limb withdrawal reflexes	L4–S3 myelopathy
2	12-year-old FN Labrador retriever	Acute-onset abnormal pelvic limb gait	Thoracolumbar back pain, ambulatory paraparesis and pelvic limb ataxia	T3–L3 myelopathy
3	10-year-old MN Labrador retriever	Acute-onset abnormal pelvic limb gait	Thoracolumbar back pain, ambulatory paraparesis and pelvic limb ataxia	T3–L3 myelopathy
4	8-year-old MN Labrador retriever	Acute-onset low neck carriage	Cervicothoracic back pain, ambulatory tetraparesis, pyrexia	C6–T2 myelopathy
5	3-year-old ME English bulldog	Acute-onset lethargy and reluctance to walk	Thoracolumbar back pain, pyrexia	None
6	11-year-old ME flat-coated retriever	Acute-onset lethargy and diarrhoea	Thoracolumbar back pain, pyrexia	None
7	6-year-old FE Cavalier King Charles	Acute-onset reluctance to rise and vocalisation	Thoracolumbar back pain, ambulatory paraparesis, pyrexia, left hind lameness	T3–L3 myelopathy
8	2-year-old FE Rhodesian ridgeback	Acute-onset lethargy and vocalisation	Thoracolumbar back pain, pyrexia	None
9	2-year-old MN border terrier	Acute-onset lethargy and tremors	Thoracolumbar back pain, pyrexia	None
10	8-year-old MN crossbreed	Acute-onset lethargy and reluctance to walk	Low neck carriage, cervical pain	None
11	5-year-old FN springer spaniel	Acute-onset lethargy	Lumbar back pain, pyrexia	None
12	2-year-old MN Irish wolfhound	Acute-onset lameness, lethargy and abnormal pelvic limb gait	Thoracic back pain, pyrexia, dysuria, lameness	C6–L3 myelopathy
13	11-month-old MN whippet	Acute-onset reluctance to walk and weight loss	Lumbar back pain, pyrexia	None
14	1-year-old ME French bulldog	Acute-onset reluctance to walk	Cervical pain, ambulatory tetraparesis, pyrexia	C1–C5 myelopathy
15	9-month-old FE British bulldog	Acute-onset lethargy, vocalisation, vomiting and diarrhoea	Thoracolumbar pain, pyrexia	None
16	8-year-old ME German shepherd dog	Acute-onset reluctance to walk and pollakiuria	Lumbar pain, pyrexia	L4–S3 myelopathy

FE, Female Entire; FN, Female Neutered; ME, Male Entire; MN, Male Neutered.

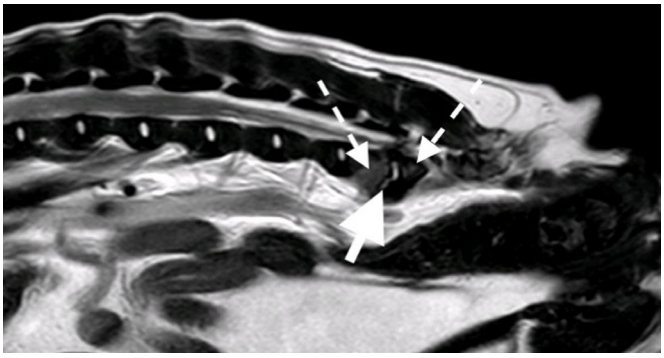

Figure 1 Sagittal T2-weighted MRI of the lumbosacral spinal cord of case 1 demonstrating the irregular hyperintense L7–S1 intervertebral disc (large white arrow) and hyperintensity of the vertebral endplates (dashed white arrows).

two were performed at surgery. Positive cultures were achieved in 27 of 74 of all samples: blood (19 of 45), urine (6 of 16) and disc aspirate (2 of 9). Sternebrae aspirates were performed in two cases with negative cultures (0 of 4). The most common bacteria cultured was *Staphylococcus pseudintermedius* (n=5); other bacteria cultured were *Escherichia coli* (4), *Streptococcus* species (3), *Staphylococcus aureus* (2), Gram-positive *Bacillus* species (2), *Staphylococcus epidermidis* (1) and *Erysipelothrix rhusiopathiae* (1). Antimicrobial treatment had been started by the referring veterinarian in four of six cases that had a negative culture. Serology for *Brucella canis* was performed in nine cases, and all were negative. Fungal culture of the blood was performed in two cases and was negative.

DISCUSSION

From this case series it was demonstrated that CRP is elevated in some, but not all, cases of diskospondylitis (87.5 per cent). An abstract published in the American College of Veterinary Internal Medicine (ACVIM) 2016 proceedings documented elevated CRP in 12 of 19 (63 per cent) cases with diskospondylitis[23]; however, the authors were unable to find a peer-reviewed manuscript of these data. The number of cases in this study with an elevation of CRP is similar to that reported in other infectious disease processes (bronchopneumonia in 12 of 16 dogs).[16] The authors found elevated CRP to be a more consistent abnormality than pyrexia, weight

Table 2 Imaging modality and disc spaces affected in each case

Case	Imaging modalities	Disc space affected
1	MRI	L7–S1
2	MRI	T12–T13
3	MRI	T13–L1
4	CT	C7–T1
5	Radiographs, CT	T9–T10
6	CT	T9–T10
7	MRI	L4–L5
8	CT	T5–T6
9	Radiographs, CT	T12–T13
10	MRI, CT	C4–C5
11	Radiographs, CT	L2–L3
12	MRI, CT	T3–T4
13	MRI	L2–L3
14	MRI	T9–T10
15	Radiographs, MRI	T11–T12
16	CT	L7–S1

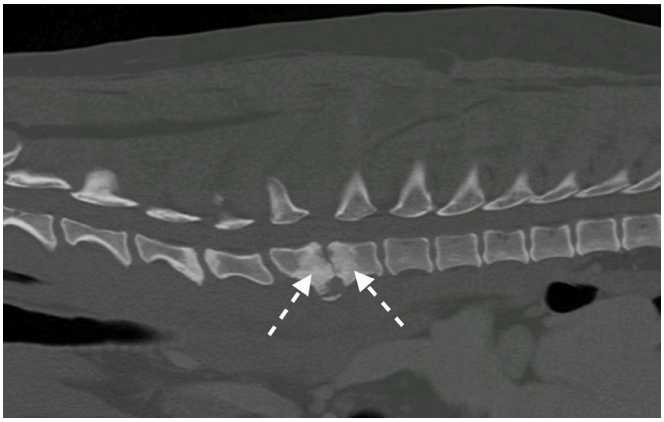

Figure 2 Sagittal CT of the cervicothoracic spine of case 4 demonstrating the irregular, osteolytic and sclerotic caudal C7 and cranial T1 vertebral endplates (dashed white arrows) and narrowing of the C7–T1 intervertebral disc space.

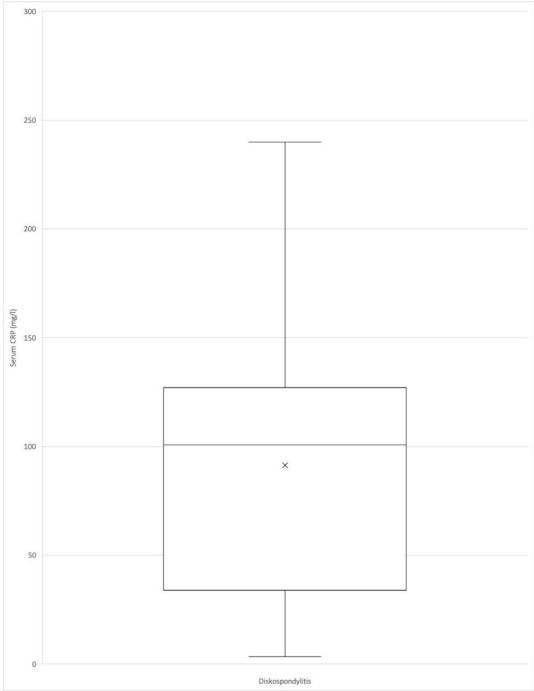

Figure 3 Serum C-reactive protein (CRP) concentrations in the 16 cases demonstrated in a box plot: median of values, minimal and maximal values, and the box contains the middle 50 per cent of sample values.

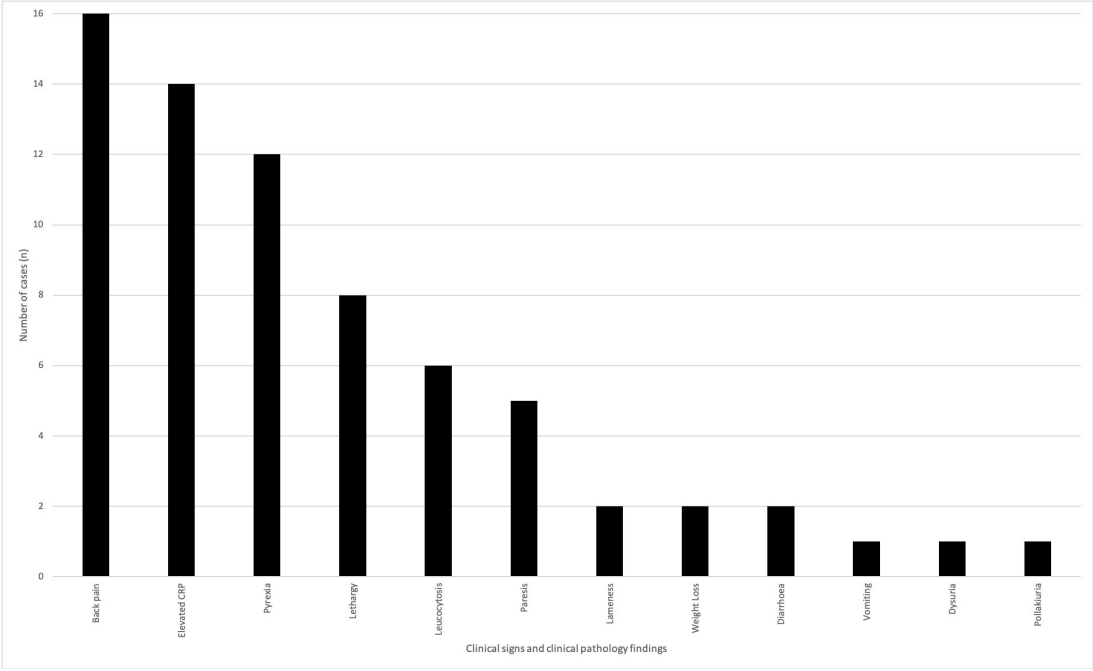

Figure 4 Bar chart demonstrating the clinical signs and clinical pathology findings in the 16 cases. CRP, C-reactive protein.

loss or haematological changes, and it could be elevated without any of the other signs other than back pain. This supported the hypothesis that CRP may be elevated in cases of diskospondylitis but more specifically in cases presenting with signs of back pain. It can be elevated despite an absence of weight loss, pyrexia or haematological changes. However, a normal CRP cannot be used to rule out diskospondylitis. CRP is used as a diagnostic biomarker in human diskospondylitis, with an increased CRP seen in 90–98 per cent of cases,[24] and demonstrated to shorten the time to diagnosis.

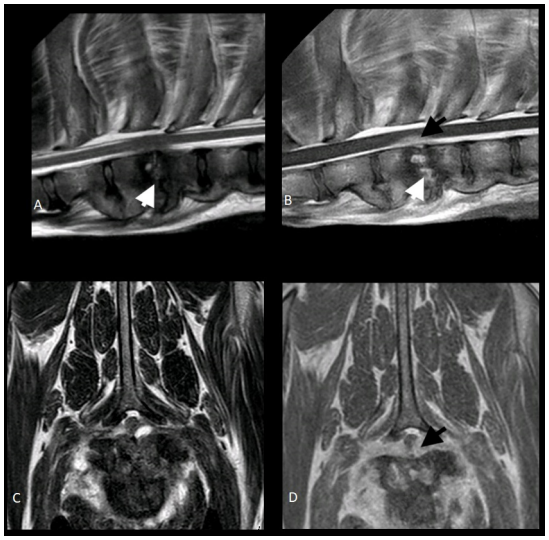

Figure 5 MRI of the thoracic spinal cord of case 12 (after recurrence of clinical signs) demonstrating the T2-weighted hyperintense and contrast-enhancing T2–T3 intervertebral disc (white arrows) consistent with diskospondylitis: (a) sagittal T2-weighted, (b) sagittal T1-weighted postgadolinium, and (c) transverse T2-wighted and (d) transverse T1-weighted postgadolinium. An extradural, mass-like compression that is contrast-enhancing can be observed in 'b' and 'd' (black arrows), which is consistent with spinal empyema.

Secondly, the authors found that CRP was lower once clinical signs had improved in dogs receiving antimicrobials. This suggests serial monitoring may have some benefit to guiding treatment choice and duration; however, the intervertebral disc is an immune privileged site and once the initial acute phase response has been addressed the entire infection may not have cleared,[25] so there is still a rationale for continuing treatment. Treatment monitoring for diskospondylitis using CRP is documented in human literature,[26] guiding the change of treatment from intravenous to oral antibiotics. The one case that suffered relapse of diskospondylitis and suspected spinal empyema following cessation of antimicrobials despite a normal follow-up CRP illustrates that normal CRP should not be used as the sole indication that treatment has been successful. In this case the outcome was severe, with euthanasia due to severe clinical pain and MRI recurrence of diskospondylitis and empyema. The remaining cases with follow-up CRP had resolution of clinical signs at the time of follow-up. Currently the mean duration of treatment in diskospondylitis has been reported to be as long as over 50 weeks,[4] with clinical signs or radiographic changes being used to monitor,[20] which is likely to be of great expense financially and increase bacterial resistance. For this reason, CRP may provide a vital future monitoring tool for these cases, similar to a prospective study using CRP to guide treatment cessation in bronchopneumonia cases in dogs.[18]

Two of the present cases had a normal CRP. In case 2 antibiotics had been started before CRP measurement,

Table 3 Serum CRP value, culture findings, follow-up CRP and prior treatment before CRP and culture

Case	CRP elevation (value in mg/l)	Urine culture	Blood culture	Disc culture	Follow-up CRP elevation	Comorbidity	Antibiotics before CRP	Antibiotics before culture
1	Yes (109.5)	Positive	Positive	N/A	No	N/A	No	No
2	No (5.2)	Positive	Positive	Negative	N/A	N/A	Yes	Yes
3	No (3.4)	Negative	Negative	Negative	N/A	N/A	No	Yes
4	Yes (139.6)	Positive	Positive	N/A	N/A	N/A	No	No
5	Yes (106.3)	Negative	N/A	N/A	No	Bilateral otitis externa	Yes	Yes
6	Yes (73.4)	Negative	Positive	N/A	No	Perianal adenoma	Yes	Yes
7	Yes (33.1)	Positive	Positive	Negative	N/A	N/A	Yes	Yes
8	Yes (121.1)	Positive	Positive	N/A	N/A	N/A	No	No
9	Yes (36.4)	Negative	Negative	Positive	No	N/A	Yes	Yes
10	Yes (164)	Negative	Positive	Negative	No	IMPA	No	No
11	Yes (128.9)	Positive	Positive	N/A	N/A	N/A	No	No
12	Yes (19.1)	Negative	Negative	Negative	No	Urinary tract obstruction	No	No
13	Yes (97.6)	Negative	Negative	Positive	No	Sublumbar foreign body	No	No
14	Yes (81)	Negative	Negative	N/A	N/A	N/A	No	No
15	Yes (103.9)	Negative	Negative	Negative	N/A	N/A	Yes	Yes
16	Yes (240)	Negative	Negative	Negative	No	N/A	Yes	Yes

CRP, C-reactive protein; IMPA, immune-mediated polyarthritis; N/A, not available.

potentially explaining the normal result. In case 3 the CRP was measured before antibiosis; however, the dog was otherwise well, so the underlying bacteraemia may have resolved and left a localised diskospondylitis. The putative theory of a negative CRP would indicate that a systemic inflammatory response may not be occurring in that patient.[12 16] In both cases the disc aspirates were performed at surgery, with degenerative neutrophils identified at cytology, suggesting a septic focus had been present. Both had been treated with antibiotics before surgery, so these may have generated a false negative for culture. This could be due to the fact that CRP can be normal even in the presence of marked inflammatory response; a study looking at CRP values in dogs with immune-mediated haemolytic anaemia reported elevated CRP values in only 86 per cent of cases (30 of 35 cases).[16]

The percentage of dogs in this study with CRP greater than 100 mg/l (10 mg/dl) was 50 per cent, which is comparable with SRMA[12 13] and IMPA.[16] It has been previously reported that other neurological diseases that might cause spinal pain[12 19] (intervertebral disc extrusion, meningoencephalitides, tumours of the CNS) do not appear to have an elevated serum CRP or only have mild elevations. However, SRMA, which can cause cervical pain particularly in young dogs, will often have a raised CRP.[12 13] Given the biphasic age presentation of diskospondylitis in dogs is geriatric and less than one year old,[4] in young dogs SRMA would still be considered a differential without further imaging.

It is possible that the CRP in some of the present cases was elevated by other comorbidities, such as urinary tract infection, neoplasia or other inflammatory diseases. CRP was elevated in eight of nine cases with negative urine culture, so this would support the assumption that the diskospondylitis and not the bacteriuria was the cause of the elevation. In case 10, IMPA is a disease known to elevate serum CRP,[16] so the origin of the increased CRP in this case is non-specific. In cases 6 and 12, perianal adenoma and urethral obstruction, respectively, have not been reported, to the authors' knowledge, to cause an increase in CRP. With case 5 bilateral otitis externa and case 13 sublumbar abscess, the authors would speculate that CRP could have been elevated and could have been the primary sites for infection (via haematogenous spread and foreign body, respectively.)

The limitations of this study include its retrospective nature (data collected retrospectively and susceptible to bias), the limited number of cases and the limited follow-up time for cases following treatment. The retrospective analysis may have generated a selection bias towards cases with more systemic signs and therefore have led to the sampling of serum CRP at the time, as 75 per cent of the dogs in this study had pyrexia. This is higher than other studies that have found the rate of systemic signs to be closer to 30 per cent.[8] The number of dogs in this case series is still relatively low, so this might be an explanation for this, as a few further normal dogs would dramatically change this percentage, or alternatively as the study is retrospective it is likely the pyrexia at presentation would then have led the clinician to check the CRP. An alternative approach to this would be to prospectively measure CRP in all cases of spinal pain to check the sensitivity and specificity of the test. Further statistical analyses were not performed due to heterogeneity of investigations and culture results in a small number of cases. Another limitation with diskospondylitis is that identifying the causative agent is not always possible, potentially due to prior use of antimicrobials or errors in sample handling, and the same can be said in human literature.[24] Blood culture, urine culture and CT or fluoroscopy-guided disc aspirate culture results[27] were reviewed and included when available.

The present findings show that CRP can be elevated in cases of diskospondylitis, even in the absence of pyrexia or leucocytosis. Further research into its diagnostic usefulness is recommended, for example, for screening cases presenting with back pain as their sole sign or to guide antimicrobial treatment duration in confirmed cases.

Contributors Planning of the study was conducted by all three authors. Data gathering was conducted by the primary author. Review of the final draft of the manuscript was performed by all authors. Tables and figures were provided by all authors.

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Competing interests None declared.

Ethics approval Ethical approval was obtained from the animal welfare and ethics board of the university (VIN/18/071).

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ORCID iDs
George Nye http://orcid.org/0000-0003-2029-2883
Francois-Xavier Liebel http://orcid.org/0000-0002-5484-1097

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