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ORIGINAL ARTICLE

Description and outcome of dogs with primary immune-mediated polyarthritis: 73 cases (2012-2017)

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Objectives: To provide a description of primary idiopathic immune-mediated polyarthritis, including long-term outcome and relapse rates, for dogs starting treatment with corticosteroids alone or corticosteroids with a second immunosuppressant.

Materials and Methods: Medical records were reviewed between January 2012 and December 2017 to identify dogs diagnosed with primary immune-mediated polyarthritis. Data including signalment, clinicopathological findings, type and duration of treatment, relapse and outcome were recorded.

Results: Seventy-three dogs were included. Fifty-four dogs were started on corticosteroid monotherapy (an additional immunosuppressant was introduced later in 27/54 dogs) and 19 dogs were treated with multi-modal immunosuppression from the outset. Ninety-five percent (69/73) of dogs responded favourably to therapy although death was attributed to immune-mediated polyarthritis in 19% (14/73) of dogs. Relapse of clinical signs was reported in 53% (39/73) dogs (31/39 while on treatment), with multiple relapses observed in 17 dogs. Complete cure (permanent withdrawal of immunosuppressive medication) was achieved in 46 dogs (63%). Overall, 81% of dogs had a well-managed disease for an extended timeframe (≥1131 days). Fourteen of 19 (74%) dogs that started treatment with multi-modal immunosuppression and 32 of 54 (59%) started on corticosteroids alone achieved a complete cure.

Clinical Significance: This study provides extended follow-up information for a large cohort of dogs with primary immune-mediated polyarthritis. Immunosuppressive therapy was discontinued in the majority of dogs but disease-associated mortality remains high.

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INTRODUCTION

Immune-mediated polyarthritis (IMPA), an inflammatory, non-infectious disease in dogs most commonly affects the carpi, tarsi, stifles and elbows, (Clements *et al.* 2004) with bilateral and symmetrical joint involvement typical (Bennett 1987). The underlying pathology is thought to centre on the deposition of circulating immune complexes in the synovium (Rondeau *et al.* 2005, Kohn 2007).

IMPA is a complex disease with multiple possible aetiologies (Clements *et al.* 2004). The most common form of IMPA is considered idiopathic and is diagnosed by exclusion of underlying infectious disease and other distant immunogenic stimuli (Stone 2017). IMPA is one of the most common causes of pyrexia of unknown origin in dogs (Chervier *et al.* 2012, Black *et al.* 2019). Affected dogs also frequently present with lameness, stiffness, joint pain and effusion, lethargy and inappetence (Rondeau *et al.* 2005) although signs may be intermittent (Clements *et al.* 2004).

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Standardised treatment protocols for primary IMPA have not been established and are derived from clinical experience or extrapolated from approaches recommended for other immune-mediated conditions. While administration of immunosuppressive doses of corticosteroids is considered the standard of care for primary IMPA (Stone 2017), an optimal protocol has not been established, with other immunosuppressive agents sometimes used in combination with corticosteroids (Archer 2017, Stone 2017). A favourable initial response to prednisolone therapy was previously described in 81% of dogs diagnosed with primary IMPA (Clements *et al*. 2004). However, 31% of these dogs subsequently relapsed, required continuous anti-inflammatory treatment, or were euthanased because of persistent disease (Clements *et al*. 2004). The impact of starting treatment with a combination of immunosuppressive medications has not been previously evaluated.

The aim of this retrospective study was to describe the signalment, clinical findings, patient pathways [whether the dogs started treatment with corticosteroids alone (steroid only or SO) or with corticosteroid and an additional immunosuppressant (multi-modal immunosuppression or MI)] and outcomes for dogs diagnosed with primary IMPA.

MATERIALS AND METHODS

Ethical approval was obtained from the University of Nottingham ethical review committee (3391 210611).

Medical records were reviewed to identify all dogs diagnosed with primary IMPA presenting to Willows Veterinary Centre and Referral Service between January 2012 and December 2017. Enrollment criteria included the presence of neutrophilic inflammation in samples of synovial fluid from three or more joints and exclusion of a potential underlying trigger of disease based on the availability of a complete blood count, comprehensive biochemical profile, imaging of the thorax (orthogonal view radiographs or CT) and abdomen (ultrasound or CT) and serological testing for tick-borne diseases (*Anaplasma phagocytophilum* and *Borrelia burgdorferi)* if the dog had a recent history of travel outside of the UK or recent detection of ticks.

For all patients with primary IMPA, the following information was collated: breed; age; sex; neuter status; bodyweight; presence or absence of specific clinical signs (lameness or stiffness; pyrexia (T > 39.2°C); lethargy; hyporexia or weight loss; joint effusion or pain and peripheral lymphadenopathy) and duration of these clinical signs before presentation. The presence or absence of thoracic or abdominal lymphadenopathy (from imaging reports), was also recorded. Initial treatment was categorised as being either corticosteroid (SO), or multi-modal immunosuppression (MI). Dogs started on corticosteroids (SO) were subdivided into those that exclusively received corticosteroid monotherapy (steroids only always – SOA) and those that had delayed (after 7 days) introduction of a secondary immunosuppressant as rescue therapy (RT). The initial treatment, including immunosuppressive medication(s) (dexamethasone, prednisolone, azathioprine, cyclosporine or mycophenolate), starting dose and frequency, was also recorded.

Referring veterinarians were contacted to provide follow-up information including up-to-date clinical records and, if relevant, date and cause of death. Owners were contacted to verify the dog's status if the dog had not visited the referring veterinarian within the previous month.

Outcome data included calculation of time to death and cause of death (classified as IMPA-related or unrelated) or time to the last follow-up; total duration of immunosuppressant therapy; occurrence and timing of relapse (recurrence of clinical signs consistent with IMPA) and the medications selected for any rescue protocol. A complete cure was defined as a sustained absence of clinical signs without the need for ongoing medication similar to a previous publication (Clements *et al*. 2004).

Statistical analysis

Cohort selection for breed predisposition calculations was performed using the total number of unique dog visits to the institution during the data collection period as the denominator. Odds ratio (OR) calculations including 95% confidence intervals were performed using an online calculator (Medcalc® statistical software: https://www.medcalc.org/calc/odds_ratio.php). Breeds in which the 95% confidence interval did not overlap 1.0 were considered to be significantly predisposed to primary IMPA (at the 5% significance level).

Histograms were used to evaluate data distributions for normality. Descriptive statistics for non-normally distributed variables were expressed as median and ranges. Categorical data were expressed as frequencies for each group.

Kaplan–Meier survival analysis was performed to evaluate disease-specific (*i.e*. attributed to IMPA) mortality using log-rank tests between groups. Disease-specific mortality was calculated by censoring deaths not attributed to IMPA. Dogs alive at the time of writing were also censored. Graphs were generated for both SO and MI groups and SOA and RT groups using SPSS (SPSS Inc.).

RESULTS

Ninety-six out of 30,519 dogs presenting to the referral centre between January 1, 2012 and December 31, 2017 were diagnosed with IMPA. Twenty-three dogs were excluded, as either thoracic or abdominal imaging had not been performed. None of the 96 animals were receiving immunosuppressive medication at the time of presentation. Thirty-three different breeds were represented including 15 crossbreed dogs (three of which were cockapoos), eight cocker spaniels, eight whippets, four miniature schnauzers, three border collies, three cairn terriers, three dachshunds, two Cavalier King Charles spaniels, two golden retrievers, two Hungarian vizslas, two Labrador retrievers, two springer spaniels and 19 other individual breeds. The proportion of dogs presenting with IMPA for each breed with more than one representative is shown in Table 1. Overall OR and 95% confidence intervals were calculated for each affected breed.

Table 1. Number of cases of immune-mediated polyarthritis (IMPA) cases per breed and total number of each breed presenting to the centre over the study period

Breed	IMPA cases	Total dogs in breed presenting to centre in this time period	Odds ratio	Confidence lower interval	Confidence upper interval
Border collie	3	903	1.4	0.4	4.5
Cairn terrier	**3**	**121**	**11.0**	**3.4**	**35.5**
Cavalier King Charles spaniel	2	838	1.0	0.2	4.1
Cockapoo	**3**	**17**	**93.2**	**26.2**	**331.3**
Cocker spaniel	**8**	**1418**	**2.5**	**1.2**	**5.3**
Crossbreed	11	3313	1.5	0.8	2.8
Dachshund	3	516	2.5	0.8	8.0
Golden retriever	2	691	1.2	0.3	5.0
Hungarian vizsla	**2**	**130**	**6.7**	**1.6**	**27.5**
Labrador retriever	2	3062	0.3	0.06	1.0
Miniature schnauzer	**4**	**403**	**4.4**	**1.6**	**12.0**
Springer spaniel	2	1099	0.8	0.2	3.1
Whippet	**8**	**184**	**21.2**	**10.0**	**44.8**

Odds ratio are presented for each breed with 95% confidence limits. Breeds displayed in bold typeface have 95% confidence intervals that do not cross 1.0 and are considered predisposed breeds

Of the 73 dogs with IMPA, there were 12 (16%) entire males, 28 (38%) neutered males, five (7%) entire females and 28 (38%) spayed females. The dogs had a median age of 4 years 6 months at presentation (range 0 years 7 months to 9 years 6 months), and a median bodyweight of 15.0 kg (range 4.5 to 46.0). Forty-eight dogs (66%) weighed <20 kg, 23 dogs (32%) between 20 and 40 kg and two dogs (3%) weighed >40 kg. The most frequent clinical signs at initial presentation were lameness/stiffness (66 dogs, 90%), pain on joint manipulation (57 dogs, 78%), pyrexia (42 dogs, 58%), lethargy (38 dogs, 53%), inappetence (33 dogs, 45%) and peripheral lymph node enlargement (24 dogs, 33%). Enlarged lymph nodes were identified in the thoracic cavity in eight dogs and in the abdominal cavity in 33 dogs. Enlargement of the medial iliac lymph nodes was specifically documented in 31 dogs. Median duration of clinical signs at the time of presentation was 30 days (range 1 to 565 days).

Fifty-four dogs were started on corticosteroid therapy only (SO) and the remaining 19 dogs started treatment with corticosteroids and azathioprine (nine), cyclosporine (six) or mycophenolate (four). Table 2 shows the signalment findings and frequencies of common clinical signs in SO and MI dogs.

Dexamethasone was administered initially in 16 of 73 dogs with a median dose of 0.3 mg/kg (range 0.2 to 0.4 mg/kg). The median starting dose of prednisolone for all 73 dogs was 2 mg/kg/day (range 0.8 to 4 mg/kg/day). The median starting dose of prednisolone was 2 mg/kg/day (range 1 to 4 mg/kg/day) for the SO dogs and 1.25 mg/kg/day (range 0.8 to 3.6 mg/kg/day) for the MI group. Where used, the starting doses of azathioprine ranged from 1.3 to 2.5 mg/kg once daily, cyclosporine from 4 to 10 mg/kg/day (divided dosing if >5 mg/kg) and mycophenolate ranged from 8 to 10 mg/kg twice daily.

In the SO dogs, a second immunosuppressant was introduced in 27 of 54 (50%), after a median of 36 days (range 7 to 226 days). Azathioprine was introduced in 18 dogs, cyclosporine in 17 dogs and mycophenolate in 12 dogs. Twenty-seven dogs were managed exclusively with corticosteroids (SOA).

Table 2. Signalment and frequency of clinical signs in dogs with primary immune-mediated polyarthritis separated according to initial treatment approach [corticosteroid monotherapy (SO) *versus* multi-modal immunosuppression (MI)]

Clinical sign	SO (n=54)	MI (n=19)
Signalment		
Age (median)	4 years 3 months	4 years 6 months
Female, n (%)	24 (44)	9 (48)
Bodyweight (kg)	13.9	18.8
Duration of clinical signs before presentation (days)	30	50
Clinical signs: n (%) of dogs		
Lameness/stiffness	52 (96)	15 (79)
Pain on joint manipulation	42 (78)	16 (84)
Pyrexia	28 (52)	15 (79)
Lethargy	27 (50)	12 (63)
Hyporexia	23 (43)	11 (58)
Peripheral lymph node enlargement	20 (37)	4 (21)

Outcome data for all 73 dogs are summarised in Fig 1. Four dogs (5%) were euthanased 7 to 33 days after starting treatment due to a failure to adequately respond. Overall, 32 (44%) dogs died or were euthanased after a median time of 1123 days (range 7 to 2931). IMPA was considered the reason for euthanasia in 14 of 32 cases. The median survival for these 14 dogs was 296 days (range 7 to 1090 days). Their median age at death was 4 years 6 months (range 1 year 0 months to 12 years 3 months). Twelve of the 14 dogs euthanased due to IMPA were in the SO group and two were in the MI group. Survival analysis is shown in Fig 2.

Relapse during or after the primary course of treatment was reported in (35/73) 48% of cases. Relapse occurred in 31 of 73 (42%) dogs during immunosuppressive therapy (after 20 to 480 days), including 17 dogs that had multiple reported relapses. Immunosuppressive medication was stopped in 49 dogs after a median of 273 days (range 38 to 1100 days). Eight of these 49 dogs relapsed 7 to 365 days after completion of the initial

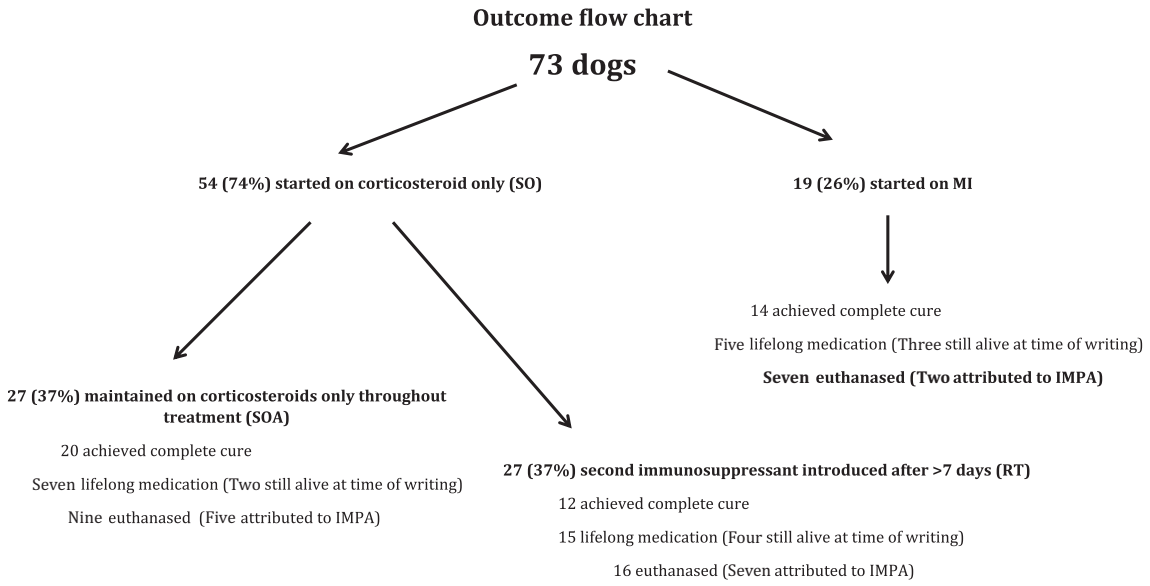

FIG 1. Outcomes for the 73 dogs presenting with primary immune-mediated polyarthritis according to the starting treatment. Dogs started therapy with corticosteroids only (SO). Dogs started on multi-modal immunosuppression (MI). Cases maintained on corticosteroid therapy only throughout treatment (SOA). Cases where a second immunosuppressant (rescue therapy) was introduced after >7 days (RT)

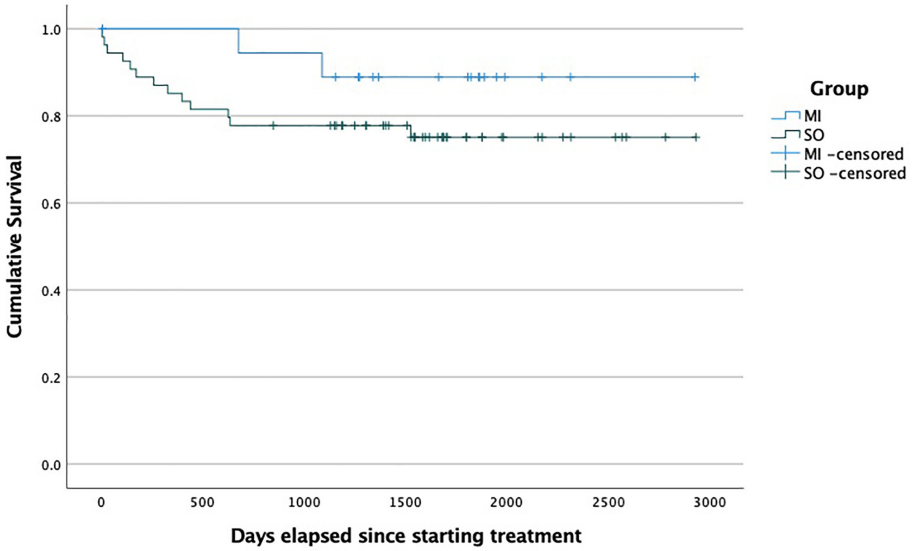

FIG 2. Survival of dogs with primary immune-mediated polyarthritis illustrated using the Kaplan–Meier method. (A) Survival curves show disease-specific mortality in 73 dogs starting therapy with corticosteroids only (SO) or with multi-modal immunosuppression (MI). (B) Survival curves showing disease-specific mortality in 54 dogs that started therapy with corticosteroids only and either remained on corticosteroid monotherapy (SOA) or had a second immunosuppressant introduced after 7 or more days (RT). Legends indicate groups corresponding to survival curve lines. Tick marks indicate censored events; dogs whose death was not associated with primary immune-mediated polyarthritis, or that were still alive at the end of available follow-up were censored from the analysis

treatment course; four of eight had previously relapsed during treatment. All eight dogs responded again to further immunosuppressive treatment, with multi-modal immunosuppression used in seven of eight cases. Five of the eight dogs were later weaned off all treatment after a median second treatment duration of 260 days (range 120 to 349). Overall a complete cure was achieved in 46 of 73 dogs (63%); follow-up of 446 to 2831 days beyond treatment withdrawal. The median available follow-up time for the 41 dogs surviving at the end of data collection was 1681 days (range 1131 to 2927).

Twenty (27%) dogs (17 SO and three MI) were treated with immunosuppressants continuously from the time of diagnosis until death (9/13 due to IMPA) or censoring (seven still alive and on treatment at the time of data collection). The median treatment duration was 1554 days (range 109 to 2589 days).

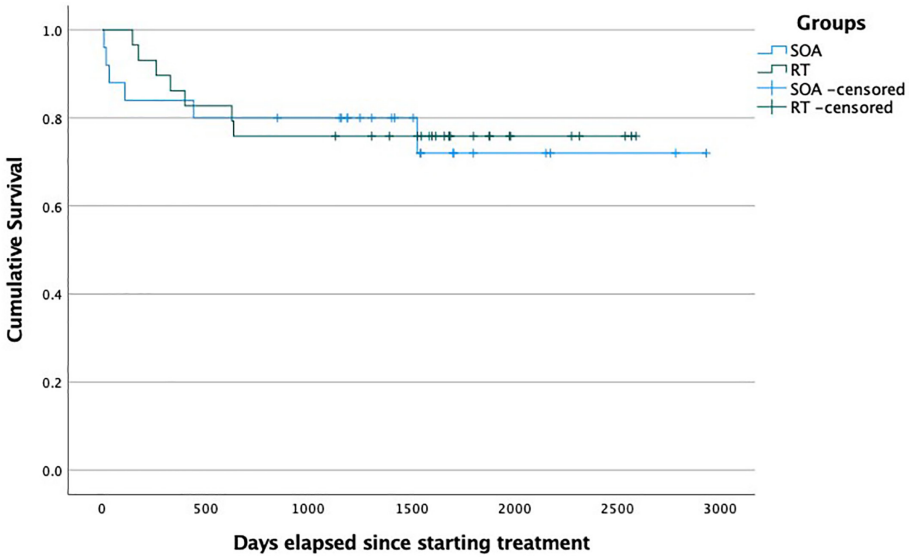

FIG 3. The Kaplan–Meier survival curve shows disease-specific mortality in 54 dogs that started therapy with corticosteroids only and either remained on corticosteroid monotherapy (SOA) or had a second immunosuppressant introduced after 7 or more days (RT). Legends indicate groups corresponding to survival curve lines. Tick marks indicate censored events; dogs whose death was not associated with primary immune-mediated polyarthritis, or that were still alive at the end of available follow-up were censored from the analysis

Fourteen of 19 MI dogs (74%) and 32 of 54 SO dogs (59%) achieved a complete cure. Of the SO group, 20 of 27 dogs in the SOA group (74%) and 11 of 27 in the RT dogs (41%) achieved a complete cure (Fig 3). Disease-specific mortality was reported in 22% of SO dogs, 11% of dogs in the MI group and in 19% of SOA dogs and 26% of the RT group.

DISCUSSION

In this study, a high proportion (95%) of dogs diagnosed with primary IMPA responded (at least temporarily) to immunosuppressive treatment with only 5% euthanased due to a failure to respond. The eventual euthanasia of 19% of dogs was attributed to IMPA, similar to mortality rates (15 to 24%) previously reported (Bennett 1987, Clements *et al.* 2004). The Kaplan–Meier curves neatly illustrate that the majority of deaths attributable to IMPA occurred in the first few months of treatment. A median survival for the cohort of euthanased dogs of 296 days suggests that even dogs that were ultimately euthanased, may be managed for extended periods. Unfortunately, assessment of the patients' quality of life during this time was not available.

A complete cure was achieved in 46 of 73 (63%) of dogs which is higher than the previously reported cure rate (Clements *et al.* 2004) but does include five dogs that required a second course of treatment due to relapse after completion of the initial therapy. The extended follow-up available here (minimum 446 days beyond completion of treatment) means that the description of complete cure can be used with confidence to describe the sustained clinical remission observed. All patients that relapsed following the withdrawal of immunosuppression did so within 1 year; relapse beyond this point is considered unlikely. Overall, continuous administration of immunosuppressive medication was more common (32%) than previously reported (18% and 11%) (Bennett 1987, Clements *et al.* 2004) with one dog receiving over 7 years of continuous immunosuppressive treatment. Whether or not such prolonged medication was warranted in every case was not established. Nonetheless, these findings do highlight a perceived need for extended treatment courses for this condition. Over half (53%) of the dogs in the study had at least one relapse, most commonly while on immunosuppressive treatment. It is possible that the clinical signs interpreted as indicative of relapse may have reflected alternate pathologies in some patients, leading to an overestimate of the true relapse rate.

In this study, cairn terriers, cocker spaniels, Hungarian vizslas, miniature schnauzers and whippets were over-represented. A predisposition to IMPA in cocker spaniels has been suggested previously (Jacques *et al.* 2002); this is a breed well recognised for developing other immune-mediated disease(s) (Threlfall *et al.* 2015, Whitley 2019). The over-representation of certain breeds suggests that genetic factors might play a role in determining susceptibility to IMPA in dogs. The other over-represented breeds identified in this study have not previously been highlighted in studies of IMPA, with the exception of the Whippet, although findings should be interpreted with caution given the low number of dogs from each breed (risk of type I error). This study did not find any evidence to support increased incidence among American Eskimo dogs as previously reported (Stull *et al.* 2008) likely due to geographic differences in breed distribution. The same rationale cannot explain the relative rarity of Labrador retrievers or German shepherd dogs in this study. The previous suggestions of predisposition in these breeds (Clements *et al.* 2004) may have been attributable to the popularity and high frequency of these breeds within the general population, rather than a real increased risk.

Similar to previous studies (Bennett 1987, Clements *et al.* 2004, Stull *et al.* 2008), no sex predilection for IMPA was found. Conflicting results have been reported regarding

the influence of size. Over-representation of both large breed (>20 kg) dogs (Clements *et al*. 2004, Rondeau *et al*. 2005) and small (<10 kg) dogs (Stull *et al*. 2008) has been reported. In this study, the median weight of dogs with IMPA was 15 kg, with a majority of dogs (66%) weighing less than 20 kg. The age predisposition in this study was very similar to previous studies (Clements *et al*. 2004, Rondeau *et al*. 2005, Stull *et al*. 2008, Stone 2017) with young to middle-age dogs most commonly affected and only six of 73 dogs aged 8 years or older at presentation. While IMPA should be considered a potential diagnosis in dogs of any sex, age, breed or size, this study provides evidence supporting an increased index of suspicion for specific breeds of young-middle age presenting with compatible clinical signs.

In this study, the most commonly reported clinical sign was stiffness, while pain on joint manipulation, pyrexia, lethargy, inappetence and peripheral lymphadenopathy were also regularly observed similar to previous reports (Bennett 1987, Clements *et al*. 2004, Rhoades *et al*. 2016). About 10% of dogs with IMPA in this study had systemic signs without reported lameness or stiffness. Dogs with polyarthritis with no obvious joint swelling or localizable pain have previously been reported in 10% to 20% of cases (Jacques *et al*. 2002, Rondeau *et al*. 2005, Rhoades *et al*. 2016). Such presentations could represent either an early stage of the disease, or overlooked/undetectable joint pain or effusion. In addition, multiple studies reported IMPA as one of the most common causes of pyrexia of unknown origin in dogs (Dunn & Dunn 1998, Chervier *et al*. 2012, Johnson & Mackin 2012, Black *et al*. 2019), suggesting that arthrocentesis should be part of the diagnostic investigation in any dog with an unexplained pyrexia, even in the absence of lameness. Onset of clinical signs before presentation was very variable (ranging from 1 to 565 days), similar to a previous publication where clinical signs commenced from 4 days to 2 years before referral (Clements *et al*. 2004). This highlights the often intermittent and non-specific nature of clinical signs associated with this condition.

Numerous IMPA treatment regimens have been proposed, either single agent protocols, or combination treatment with corticosteroids, cytotoxic drugs, or other immunosuppressive drugs (Clements *et al*. 2004, Colopy *et al*. 2010, Johnson & Mackin 2012, Rhoades *et al*. 2016). Corticosteroids have a rapid onset of action (Whitley & Day 2011, Viviano 2013, Archer 2017), which is particularly useful in a disease that can cause pain and systemic inflammation. However, corticosteroids have the potential to cause significant adverse effects that can impact the quality of life of patients and owners alike (Whitley & Day 2011, Archer 2017).

Efficacy of individual drugs or dosages is difficult to assess when multiple medications are used in combination. A prospective randomised clinical trial that included 20 dogs compared the efficacy of prednisone and cyclosporine for the treatment of primary IMPA and found a 70% positive response to treatment to both medications (Rhoades *et al*. 2016). A retrospective study that included 14 dogs with IMPA treated with leflunomide found an initial resolution of clinical signs in 57%, partial response in 35% and no response in 7% of dogs, but there was no follow-up information available relating to relapse after the initial improvement (Colopy *et al*. 2010).

In this study, the proportion of MI dogs achieving a complete cure was higher (74%) than the proportion of SO dogs (59%). This finding has relevance to therapeutic decision making and warrants further investigation *via* prospective studies. The MI group was inherently heterogeneous in terms of drug used. Dogs in the MI group were more frequently pyrexic at presentation; it is possible that the presence of pyrexia may have been interpreted as an indication of greater disease severity influencing the initial treatment selection. However, the rationale behind the selection of combination therapy could not be determined retrospectively. A selection bias may be present whereby a multi-agent approach was preferred in more severely affected dogs or, in cases where a poorer tolerance of corticosteroids was anticipated. The lower median dose of prednisolone in the MI group median 1.25 mg/kg/day would support this latter hypothesis.

In contrast to the above findings, complete cure was achieved less frequently in dogs that received a secondary immunosuppressant as a RT than dogs who remained solely on corticosteroid treatment. This paradoxical finding could reflect selection bias as dogs requiring RT, would by definition be expected to be doing more poorly, making a complete cure less achievable. Prednisolone was previously used alone in 68% of dogs and in combination with cyclophosphamide in 32%, with no difference in outcome (Bennett 1987). In the treatment of immune-mediated hemolytic anaemia, the mortality rate was reported to be similar when using multiple immunosuppressive drug treatments *versus* a single immunosuppressive drug (Grundy & Barton 2001).

In this study, relapse was defined based on recurrence of compatible clinical signs which may lead to an over-estimation of the relapse rate as some dogs may have had alternative causes for such a recurrence. Repeat evaluation of synovial fluid samples may be recommended to confirm relapse (Clements *et al*. 2004) but is rarely performed. A role for C-reactive protein (CRP) as a surrogate marker of synovial inflammation and disease activity in dogs with primary IMPA has been suggested as CRP has a high specificity for detecting poorly controlled dogs (Grobman *et al*. 2017).

Relapse during or after the primary course of treatment was reported in (35/73) 48% of cases. This is similar to what has been previously reported, with relapses occurring at any time during tapering or after discontinuing the medications (Clements *et al*. 2004). Relapse after completion of initial therapy was rare (8/49, 16%) mirroring the decreasing rates of relapse with time in dogs with thrombocytopaenia (Simpson *et al*. 2018).

This study has several limitations, inherent to its retrospective nature. Treatment protocols, monitoring and tapering schedules were not standardised; cases were managed by members of the internal medicine, orthopaedic and neurology teams and treatment choice may have been influenced by individual clinician preference as well as patient factors. Furthermore, while the attribution of death to IMPA was evident, it was impossible to ascertain retrospectively, the relative influence of disease progression and the presentation of adverse effects in reaching these decisions. Not all records provided sufficient information to determine the

details of the tapering schedule, degree of owner adherence or the timing of follow-up appointments, which may all influence the likelihood of relapse. Furthermore, joint radiography was not considered an inclusion criteria for this study. Cases of erosive IMPA, which is known to have a worse prognosis than the non-erosive form, may have been unknowingly included (Ralphs *et al*. 2000, Shaughnessy *et al*. 2016). Given the low prevalence of tick-borne diseases in the UK, serological testing was not routinely performed, unless the dog had a history of foreign travel. Finally, some dogs may have received medications in addition to the immunosuppressants, including antimicrobials, non-steroidal anti-inflammatories and antacids, before or after the diagnosis of IMPA. While it is considered highly unlikely that any of these drugs affected the outcome, it is impossible to confirm their precise impact.

In conclusion, this study suggests a reasonable to fair prognosis for primary IMPA, with 63% of dogs achieving clinical cure. The potential clinical benefit from using multi-modal immunosuppression from the outset of therapy warrants further investigation *via* a prospective study using the standardised treatment and follow-up protocols.

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.

Author contributions

Sara Ravicini: Data curation (lead); investigation (equal); supervision (equal); validation (equal); writing – original draft (lead); writing – review and editing (equal). **Andrew Kent:** Conceptualization (equal); data curation (equal); formal analysis (equal); methodology (equal); project administration (equal); supervision (equal); validation (equal); writing – review and editing (equal). **Mark Dunning:** Writing – review and editing (supporting). **Stephen Baines:** Data curation (equal); writing – review and editing (supporting). **Steven Clarke:** Writing – review and editing (supporting). **Fergus Allerton:** Conceptualization (lead); data curation (equal); formal analysis (equal); investigation (equal); project administration (lead); supervision (lead); writing – review and editing (equal).

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