PAPER

Long-term outcome of primary immune-mediated thrombocytopenia in dogs

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Objectives: To determine the incidence of relapse after discharge from the hospital in dogs with a diagnosis of presumed primary immune-mediated thrombocytopenia, risk factors associated with relapse and whether or not indefinite use of immunosuppressive medication influences risk of relapse.

Materials and Methods: Medical records from August 2007 through July 2016 were reviewed to identify dogs with a diagnosis of presumed primary immune-mediated thrombocytopenia. Data collection included signalment, initial diagnostic tests, treatment, incidence of relapse, survival duration and follow-up testing.

Results: A total of 45 dogs were diagnosed, treated and monitored for at least one year for presumed primary immune-mediated thrombocytopenia. 89·6% of patients survived to discharge and 31% of those experienced a relapse following discharge. The median time from diagnosis to relapse was 79 days. Of dogs that experienced a relapse, 50% had at least one further relapse. There was no difference in age, body weight, gender, breed, platelet count at presentation, nadir packed cell volume during hospitalisation, incidence of melaena or initial treatment between the relapsing and non-relapsing groups. In the relapsing group, time to platelet recovery was significantly longer and these patients were more likely to have received a blood transfusion.

Clinical Significance: This study does not provide evidence to support the use of long-term immunosuppressive medications to prevent relapse. However, the data suggest that patients with more severe disease at the time of diagnosis or that have already experienced a relapse should be monitored more closely.

Journal of Small Animal Practice (2018) **59**, 674–680
DOI: 10.1111/jsap.12912

Accepted: 15 June 2018; Published online: 13 August 2018

INTRODUCTION

Immune-mediated thrombocytopenia is one of the most common causes of thrombocytopenia in dogs (Botsch *et al.* 2009). In patients with immune-mediated thrombocytopenia, autoantibodies adhere to the platelet surface, leading to an increased clearance by the reticuloendothelial system and a decrease in platelet numbers (Kristensen *et al.* 1992, Scott *et al.* 2001, Wilkerson *et al.* 2001). Dogs are considered at risk of spontaneous haemorrhage when platelets counts are less than 30 to 50×10^9/L (Putsche & Kohn 2008, Scuderi *et al.* 2016). A diagnosis of primary immune-mediated thrombocytopenia can be made only after ruling out potential underlying causes (Lewis & Meyers 1996, O'Marra *et al.* 2011).

Short-term survival rates ranging from 74 to 97% have been reported for patients with immune-mediated thrombocytopenia, with melaena or a high blood urea nitrogen being associated with worse outcomes (Williams & Maggio-Price 1984, Putsche & Kohn 2008, O'Marra *et al.* 2011). In one recent study, only 9% of patients underwent a relapse, although other reported

recurrence rates have ranged from 26 to 47% (Jans *et al*. 1990, Putsche & Kohn 2008, O'Marra *et al*. 2011). Immunosuppressive drugs are the mainstay of treatment, with corticosteroids being the first-line therapy. Previous studies have evaluated the use of other immunosuppressive agents and, while vincristine and human intravenous immunoglobulin have been shown to accelerate platelet recovery time and decrease hospitalisation time, no long-term survival benefit has been demonstrated for the use of any other drug over treatment with corticosteroids alone (Bianco *et al*. 2009, Balog *et al*. 2013, Cummings & Rizzo 2017).

We hypothesised that the long-term use of immunosuppressive medications would not help to prevent relapse in dogs with primary immune-mediated thrombocytopenia. Our objective was to further evaluate the incidence of relapse for dogs with immune-mediated thrombocytopenia, to identify any possible risk factor associated with relapse, and to specifically test whether discontinuation of immunosuppressive medications would increase the risk of relapse.

MATERIALS AND METHODS

A search of the computerised medical records at our institution was performed to identify all dogs in which a diagnosis of presumed primary immune-mediated thrombocytopenia was made between August 2007 and July 2016. A platelet count of less than 150×10^9/L was initially used as a criterion for inclusion, but all cases with a diagnosis of primary immune-mediated thrombocytopenia presented with an initial platelet count of less than 40×10^9/L. Platelet counts were confirmed by review of blood smears by a clinician in all cases. Dogs with evidence of an underlying cause based on a review of the patient history, abdominal ultrasound or radiographs and tick serology testing were excluded. A minimum of a negative in-house ELISA for *Ehrlichia canis* and *Anaplasma phagocytophilum* was required although many dogs had more extensive testing for tick-borne disease. Dogs were not excluded if they tested positive for antibodies against *Borrelia burgdorferi*. Dogs were excluded from the study if they had incomplete records or if they did not meet the testing requirements to investigate for underlying disease. All dogs were newly diagnosed cases of immune-mediated thrombocytopenia, and had not previously received immunosuppressive medications for this condition.

All records were reviewed for data including time to initial response to treatment, time to remission, medications given and time to any relapse. Initial response to treatment was defined as an increase in the platelet count to greater than 40×10^9/L, at least three platelets seen *per* high powered field on a blood smear, or any platelet clumps seen on the feathered edge of a blood smear. Remission of disease was defined as a platelet count greater than 150×10^9/L. Relapse of disease was defined as a decrease in platelet count to less than 150×10^9/L.

Dogs were considered not to have relapsed if the platelet count remained above 150×10^9/L for the duration of available follow-up, as long as that follow-up was for at least one year. Dogs that did not relapse but for which follow-up was available for less than 1 year were included in the analysis for initial remission and survival to discharge, but not in the analysis of relapse. Any dog that experienced a relapse at any time during or after treatment was classified as a relapse.

To investigate whether long-term immunosuppressive treatment had a protective benefit in reducing the incidence of relapse, the relapse rate was compared between dogs that received indefinite treatment to those that received finite treatment. A dog was considered to have received indefinite treatment with a medication if that medication was still being administered at the time of last follow-up. Dogs were considered to have received finite treatment with a drug if that drug had been discontinued before the end of the study. A potential confounding factor in this analysis was that indefinite treatment might have been elected, not to prevent a possible relapse, but because one had already occurred. To reduce this confounding effect, dogs that were treated indefinitely but had experienced a relapse at a time when most dogs in the finite treatment group were still receiving medication were considered to have had an "early relapse" and were excluded from this analysis. In this case, indefinite treatment was presumed to be a result of the early relapse. Additionally, dogs were only included in the finite treatment group if they had not undergone a relapse before that medication was discontinued.

Data were analysed using a commercial computer software program (Wizard for Mac). Student's *t*-test was used to compare continuous variables between groups. The Chi-squared test was used to compare categorical variables. Statistical significance was set at a $P<0{\cdot}05$.

RESULTS

Short-term outcome

Sixty-seven dogs fulfilled the criteria for inclusion to the study, of which 60 (89·6%) survived to be discharged from the hospital, and 58 (86·6%) achieved remission of their disease. Of the seven dogs that did not survive to discharge, six were euthanased and one underwent cardiorespiratory arrest on the second day of hospitalisation. Of the two dogs that survived to discharge but did not achieve remission, one was euthanased 41 days after diagnosis and one was still alive at follow-up with a platelet count less than 150×10^9/L at 933 days after diagnosis. One-year mortality rate from all causes was 19·4% and that from presumed immune-mediated thrombocytopenia was 11·9%.

Relapse rate

Forty-five of the 58 dogs that achieved remission were able to be assigned to the relapse or non-relapse groups (see Fig. 1). Of those 45 dogs, the results of an abdominal ultrasound examination were available for review in 44 (abdominal radiographs were available in the dog for which an abdominal ultrasound was not performed) and thoracic radiographs were available in 42 dogs. Screening for vector-borne diseases comprised in-house ELISA (Snap 4Dx, Idexx – includes *Ehrlichia canis*, *Anaplasma phagocytophilum*, *Borrelia burgdorferi* and *Dirofilaria immitis*) in 11 dogs, in-house ELISA and IFA testing for antibodies against multiple agents (*Babesia*

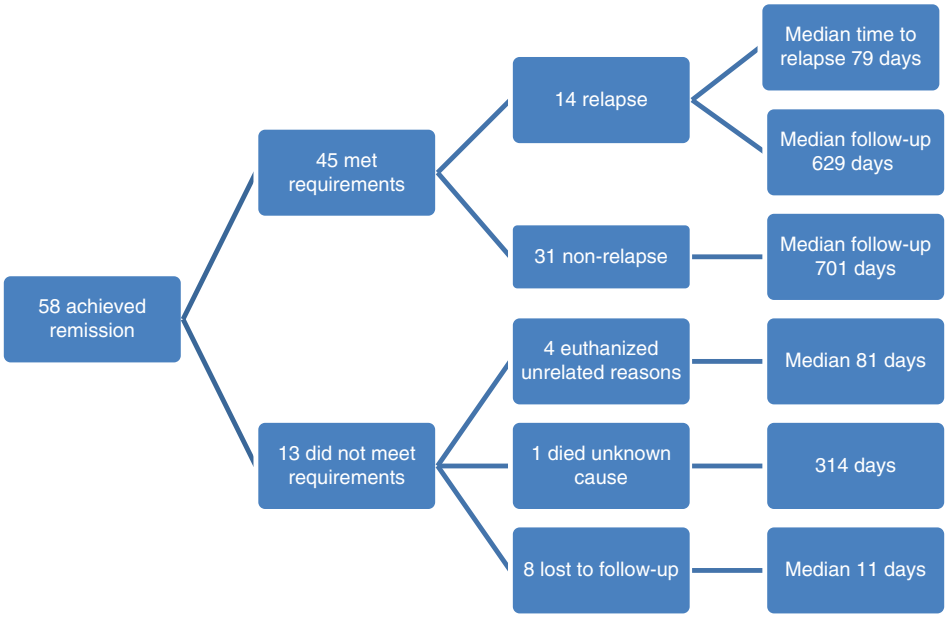

FIG 1. Summary of dogs that met requirements and experienced relapses"Did not meet requirements" refers to dogs that did not have follow-up beyond 1 year of diagnosis; "met requirements" refers to dogs that met the minimum one year of follow-up inclusion criteria of the study

canis, *Babesia gibsonii*, *Bartonella koehlerae*, *Bartonella hensalae* *Bartonella vinsonii*, *Ehrlichia canis* and *Rickettsia rickettsiae*) in 17 dogs and PCR testing for multiple agents (*Anaplasma phagocytophilum*, *Anaplasma platys*, *Babesia canis*, *Babesia gibsoni*, *Bartonella henselae*, *Bartonella vinsonii*, *Ehrlichia canis*, *Mycoplasma haemocanis*, *Neorickettsia risticii*, *Rickettsia rickettsii*) in 17 dogs. In all dogs, the results of these additional studies failed to reveal any potential underlying cause for the thrombocytopenia. Of the 13 dogs that did not fulfil the criteria for the relapse or non-relapse groups, four were euthanased for reasons unrelated to immune-mediated thrombocytopenia at a median of 81 days after diagnosis (range 9 to 315 days), one died of unknown causes at 314 days, and eight were lost to follow-up at a median of 11 days after diagnosis (range 0 to 228). Of the 45 dogs that met the requirements for inclusion for evaluation of relapse rate 14 (31·1%) experienced a relapse and 31 (68·9%) did not relapse. The median time to relapse was 79 days (range 15 to 1239). 78·6% of the dogs that relapsed did so within 1 year from presentation. A median of 701 days of follow-up (range 399 to 2755) was available for the non-relapsing group. Median follow-up time available for the relapsing group was 629 days (range 367 to 2040). Median platelet count at relapse was 33×10^9/L (range 0 to 113×10^9/L).

Comparison of relapse and non-relapse groups

Comparing the relapse and non-relapse groups, there was no difference in age, body weight, gender status or breed between the relapse and non-relapse groups (see Table 1). The two groups had similar platelet counts at the time of presentation but the time to platelet recovery was significantly longer in the relapse group. There was no difference in nadir PCV or the incidence of melaena between the two groups. However, 10/14 (71·4%) dogs in the relapse group received at least one transfusion compared to 12/31 (38·7%) in the non-relapse group.

There were no statistically significant differences in initial treatment between the two groups. Vincristine was given to 10/14 (71·4%) of dogs within the relapsing group and 20/31 (64·5%) of dogs in the non-relapsing group. All dogs were receiving prednisone at the time of discharge with no significant difference in dose between the relapse and non-relapse groups. Mean dose of prednisone for all dogs was 2·1 mg/kg per 24hours. In the non-relapsing group, 24/31 (77·4%) dogs had been started on a second immunosuppressive agent at the time of discharge (cyclosporine n=4, mycophenolate n=4, azathioprine n=16). Thirteen of 14 (92·8%) of dogs in the relapse group had been started on a second immunosuppressive agent (cyclosporine n=3, azathioprine n=10) at the time of discharge. There was no significant difference between the groups in the number of dogs treated with a second immunosuppressive agent. Mean dose of azathioprine at discharge was 1·8 mg/kg *per* 24 hours, cyclosporine was 8·3 mg/kg every 12 hours and mycophenolate was 12·4 mg/kg every 12 hours. Tapering rates for prednisone and other immunosuppressives were not known for all dogs because some dogs were followed by the referring veterinarian after discharge from our facility.

Treatment at relapse

There were 14 dogs that experienced a relapse. Of these, four (28·6%) were not receiving any immunosuppressive treatment at the time of relapse. The remaining 10 dogs (71·4%) were still receiving treatment with prednisone or prednisone and an additional immunosuppressive drug at the time of relapse. Nine of these dogs were also on a second agent at the time of relapse (azathioprine n=6, cyclosporine n=3). No dog in the relapse groups was on a second agent alone at the time of relapse. The median time between discontinuation of prednisone and relapse was 70 days. Four dogs had the second agent discontinued before

Table 1. Comparison of variables between relapsing and non-relapsing groups

Variables	Relapse	Non-relapse
Follow-up/days (range)	701 (399 to 2755)	629(367 to 2040)
Age/months (range)	92 (18 to 151)	76 (31 to 156)
Sex	6 CM, 8 FS	19 CM, 12 FS
Breed	Akita 1	Bichon Frise 2
	Dachshund 1	Border collie 2
	Gordon setter 1	Boxer 1
	Great dane 1	Cocker spaniel 4
	Pitbull 2	Corgi 1
	Pomeranian 3	Golden retriever 1
	Poodle 3	Hovawart 1
	Rat terrier 1	Labrador retriever 3
	Scottish terrier 1	Maltese 1
		Mixed 1
		Pekingese 1
		Pomeranian 3
		Poodle 3
		Pug 1
		Rottweiler 2
		Shih-tzu 1
		Vizsla 1
		Welsh terrier 1
		Yorkshire terrier 1
Weight (kg)	20·5 (4·5 to 65)	15 (3 to 55)
Plts at presentation ($\times10^9$/L)	10 (2 to 34)	19 (0 to 37)
PCV nadir (%)	19 (12 to 46)	28 (11 to 46)
Melena (2 cases NA)	No 6	No 17
	Yes 6	Yes 14
Transfusion	No 4	No 19
	Yes 10	Yes 12
Number of transfusions	1 (0:5)	0(0:6)
Vincristine	No 4	No 11
	Yes 10	Yes 20
Time for plts to recover to ≥40×10^9/L (days)	6·5 (3 to 21)	4 (1 to 12)
Percent that were > 40×10^9/L at discharge	71·4% (10/14)	74·2% (23/31)
Second agent (any)	13/14	24/31
Time from dx to plts in RR (days)	11 (5 to 25)	9 (2 to 20)
Hospitalisation time (days)	4·5 (0 to 11)	4 (0 to 9)
Plt count at discharge ($\times10^9$/L)	56 (15 to 200)	67·5 (0 to 200)
Plts at first recheck ($\times10^9$/L)	410 (52 to 1492)	425 (0 to 1637)
Plts at second recheck ($\times10^9$/L)	173 (4 to 1000)	326 (109 to 901)

CM Castrated male, FS Female spayed, kg kilograms, Dx diagnosis, Plts Platelets, PCV Packed cell volume, RR reference range, NA Not applicable

relapse. The median time between discontinuation of a second agent and relapse was 79 days (range 48 to 684).

Effect of finite *versus* indefinite treatment with prednisone

Prednisone was discontinued before the end of the study period in 24/45 dogs (53·3%) after a median of 116 days (range 58 to 645 days; see Fig. 2). These patients were considered to have received finite treatment. One dog was excluded from the finite treatment group since it had relapsed 15 days after diagnosis; prednisone was discontinued 120 days later. In the remaining 23 dogs that received finite treatment with prednisone, the median follow-up time after discontinuing prednisone was 579 days (range 267 to 2321 days). A relapse occurred after discontinuing prednisone in three out of 23 (13·0%) dogs. In these three dogs, prednisone had been discontinued after 74, 79 and 116 days of treatment; relapse occurred 6, 70 and 647 days after discontinuing prednisone, respectively. Twenty-one of 45 (46·7%) dogs received indefinite treatment with prednisone (median follow-up time 640 days, range 367 to 2040). Six dogs were treated indefinitely after experiencing a relapse at ≤116 days after diagnosis and were excluded (116 days was the median duration of treatment for the finite treatment group). After excluding these dogs, a relapse occurred in four out of 15 (26·6%) dogs in the indefinite treatment group, at a median time after diagnosis of 987 days, (range 498 to 2040 days). There was no significant difference in the rate of relapse between the dogs receiving finite treatment (relapse rate 13%) and those receiving indefinite treatment (26·6%).

Effect of finite *versus* indefinite treatment with any immunosuppressive drug

All immunosuppressive drugs had been discontinued before the end of the study period in 20/45 dogs (44·4%), after a median of 137 days (see Fig. 3). These patients were considered to have received finite treatment. The same dog that was excluded from the finite prednisone treatment group was excluded again. A relapse occurred after discontinuing treatment in 3/20 (15%) dogs in the finite treatment group. In these three dogs, immunosuppressive treatment had been discontinued after 74, 93 and 116 days of treatment; relapse occurred 48, 70 and 684 days, respectively, after discontinuing treatment. Twenty-five of 45 (55·6%) received indefinite treatment with at least one immunosuppressive drug (median 640 days, range 367 to 2040 days). Nine dogs were treated indefinitely after experiencing a relapse at ≤137 days after diagnosis and were excluded. After excluding these dogs, a relapse occurred in three out of 16 (18·9%) dogs in the indefinite treatment group, at a median time after diagnosis of 496 days (range 213 to 1239). There was no significant difference in the rate of relapse between the dogs receiving finite treatment (relapse rate 15%) and those receiving indefinite treatment (18·9%).

Subsequent relapses

Of the 14 dogs that relapsed, seven developed a second relapse, and two dogs went on to develop three or more relapses. Median time to relapse for dogs who only relapsed once during the course of the study was 149 days (range 15 to 1239), and the median time to relapse for the dogs that developed multiple relapses was 78 days (range 34 to 231). Of the seven dogs that experienced a second relapse, five were receiving immunosuppressive medications at the time of the second relapse. For third and subsequent relapses, all dogs were receiving immunosuppressive medications at the time of relapse. Of the seven dogs that experienced more than one relapse, four were alive at the time of last follow-up a median of 1008 days (range 655 to 1389) after presentation and 853 (577 to 1355) days after the second relapse, two dogs died of unrelated causes (at 401 and 640 days after initial presentation), and one dog was euthanased due to frequent relapse at 367 days after initial presentation at which time it had undergone five relapses.

Long-term outcomes

Nine of the 14 dogs (64·3%) that relapsed were still alive at the time of last follow-up, a median of 603 days (range 255 to

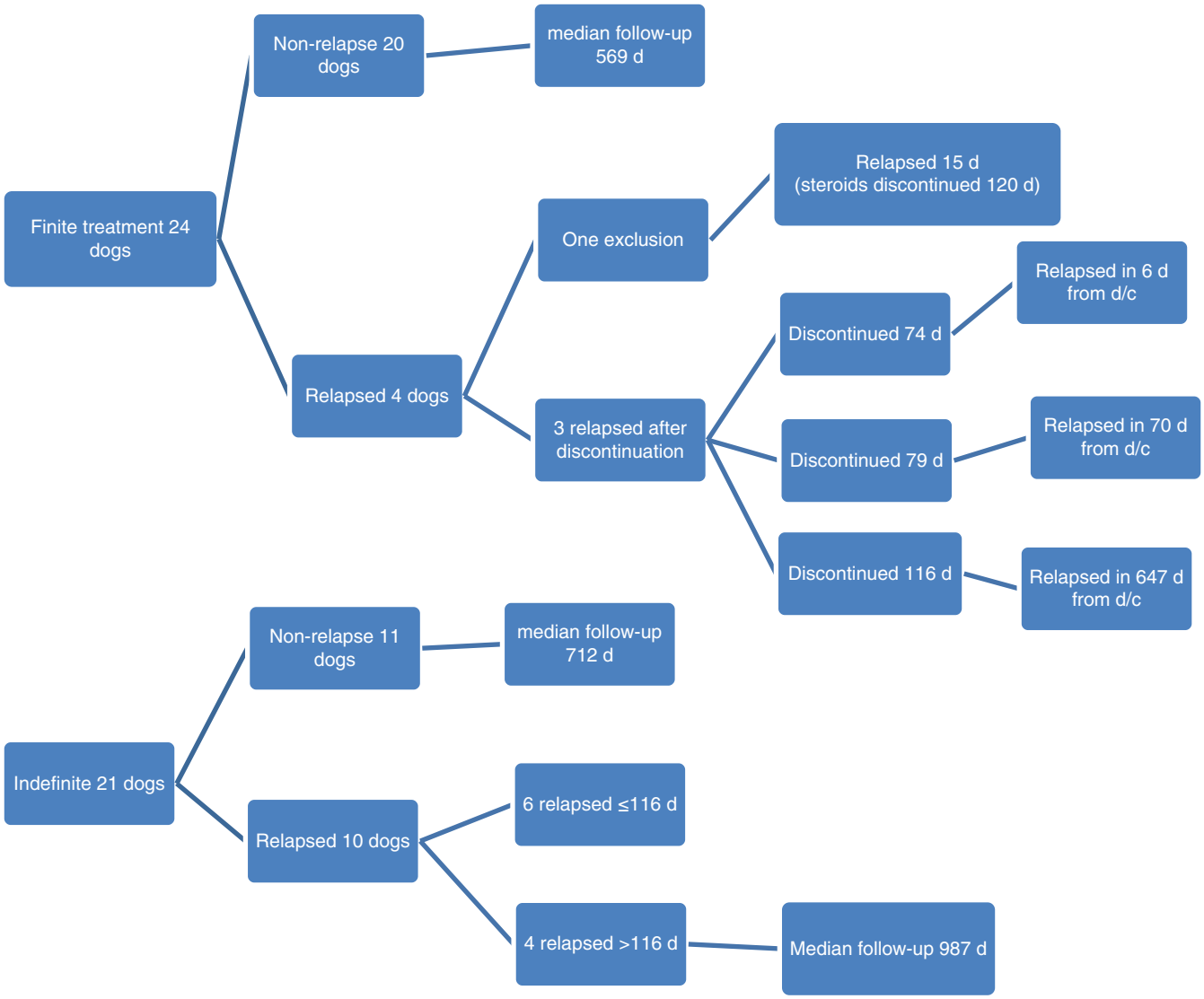

FIG 2. Prednisone treatment (finite *versus* indefinite); Median treatment discontinuation was 116 days. D days, d/c discontinuation

1355 days) after their initial relapse. Four dogs were euthanased at a median of 417 days (range 2 to 597 days) after relapse. One dog died of unknown causes 321 days after relapse. Twenty-six of 31 dogs (83·9%) in the non-relapse group were still alive at a median of 675 days (range 399 to 2755) and five out of 31 had been euthanased at a median of 1052 days (range 528 to 1394). Overall, 35 of 45 dogs (77·8%) were still alive at the end of the study.

DISCUSSION

The overall prognosis for presumed immune-mediated thrombocytopenia in this study was good, with 89·6% patients surviving to discharge and 86·6% achieving a remission of their disease. Among patients for which long-term follow-up was available, relapse occurred in 31%. A recent case series including 54 dogs (that survived to discharge and were not lost to follow-up) found a relapse rate of only 9% (O'marra *et al.* 2011), although previous studies with fewer dogs have found relapse rates from 26% (Putsche & Kohn 2008) to 47% (Jans *et al.* 1990). Differences in reported relapse rates could be due to differences in duration of follow-up, differences in criteria chosen to define a relapse, differences in treatment protocols or inclusion of dogs with other underlying disease. The current study also showed that 50% of dogs that relapsed went on to have another relapse.

The follow-up duration in the current study was selected to reduce the likelihood that a patient would be incorrectly assigned to the non-relapsing group. It is still possible that dogs undergoing a relapse after 1 year could have been incorrectly assigned to the non-relapse group. However, initial relapses occurred at a median of only 79 days after initial diagnosis and 78·6% dogs that relapsed had done so within 1 year. Moreover, the median follow-up time significantly exceeded the initial inclusion criteria at 701 days (399 to 2755) for the non-relapsing group.

The platelet count 'cut off' for a relapse of 150×10^9/L was chosen in this study to maximise the sensitivity for detecting a relapse and could have over-estimated the relapse rate. However,

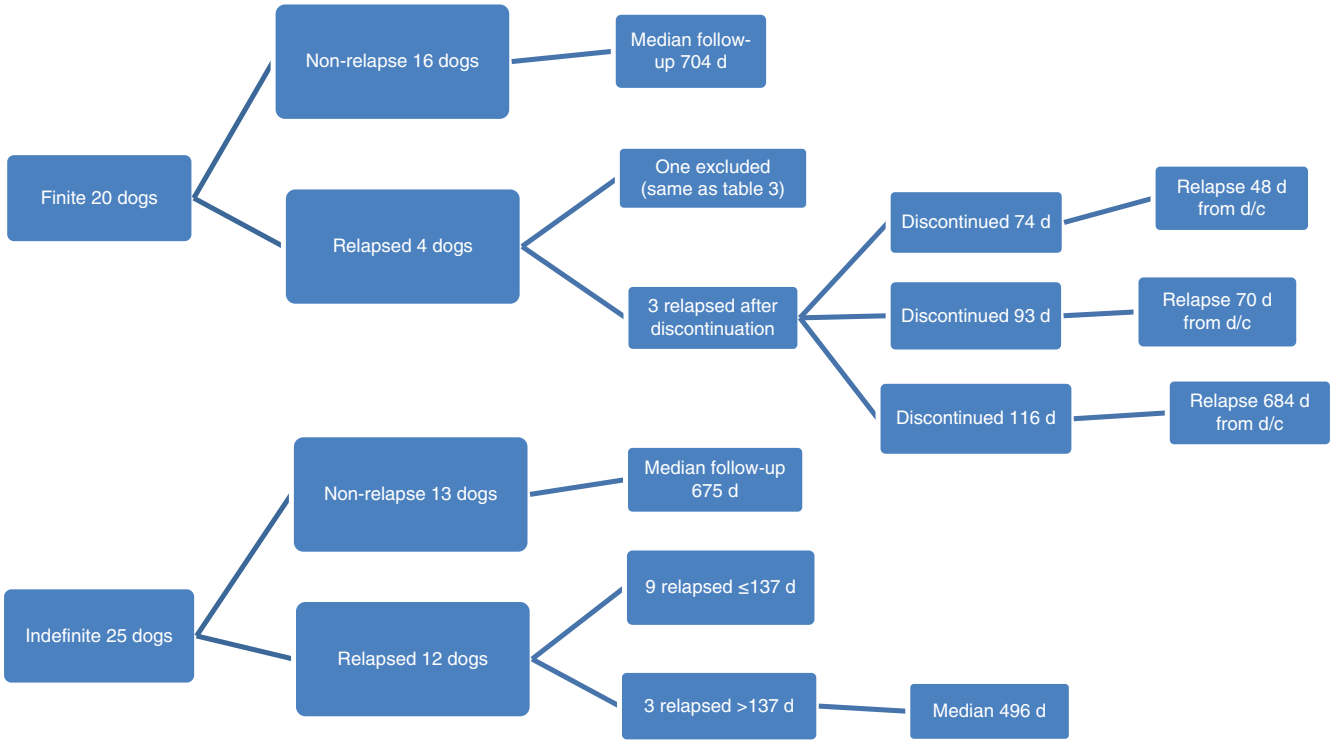

FIG 3. Any immunosuppressive (finite *versus* indefinite); median treatment discontinuation was 137 days. D days, d/c discontinuation

all dogs in the relapse group ultimately had a platelet count of less than 100×10^9/L, and it is unlikely that this change simply represented a fluctuation.

It is possible some dogs may have relapsed because of an undetected underlying infectious or neoplastic disease. It is common at our hospital for dogs to be treated empirically with doxycycline while the results of testing for exposure to or infection with infectious agents are pending, and this may have resulted in an initial response with later relapse when the doxycycline was withdrawn. This is unlikely given the majority of these animals either had negative tick testing or were treated with a course of doxycycline for at least 2 weeks.

Our results suggest that not only is the short-term prognosis for presumed immune-mediated thrombocytopenia good with appropriate treatment, but that the mortality of relapsing dogs was low. Moreover, although late relapse is also possible, the likelihood of relapse for dogs still in remission at 90 and 180 days decreases to 15·8% and 11·1%, respectively.

It is possible that differences in treatment protocols could lead to differences in recurrence rates between studies. However, no differences in initial treatment between the relapsing and non-relapsing groups were identified. The doses of prednisone fell into the range considered as immunosuppressive with a mean dose of 2·1 mg/kg per 24 hours (Jans *et al.* 1990, Lewis & Meyers 1996). The majority of the dogs within this study were also treated with an additional immunosuppressive agent. Our data failed to show any benefit of a second immunosuppressive agent in reducing the frequency of relapse. However, the number of dogs receiving any particular medication was low and any treatment benefit would have been difficult to identify. Other studies have been unable to show a significant association with survival or relapse and specific treatment protocols (Williams & Maggio-Price 1984, Jackson & Kruth 1985, Jans *et al.* 1990, Lewis & Meyers 1996, Rozanski *et al.* 2002, Putsche & Kohn 2008, Nakamura *et al.* 2012, Scuderi *et al.* 2016, Cummings & Rizzo 2017). Inadequate treatment is also unlikely to be contributing to overestimated recurrence rates, given that our study showed similar survival rates (short 89·6% and long 80·6%) when compared to previously reported studies [74% (Williams & Maggio-Price 1984), 84% (O'Marra *et al.* 2011) and 97% (Putsche & Kohn 2008)].

The initial aim to evaluate discontinuation of immunosuppressive medications on the incidence of relapse was difficult to investigate since some relapses occurred before medications had been discontinued. When considering only dogs that relapsed after discontinuation to dogs that received indefinite treatment without relapse, no significant benefit of indefinite treatment was found. The number of cases available for this analysis was small, and the power of the study to identify a benefit of a specific treatment protocol would have been low. Regardless, the study suggested that the benefit of indefinite treatment was low with a relapse occurring after discontinuation of all medications in 18·9% dogs compared to 20% of dogs that were treated with indefinite medications. Moreover, most relapses occurred early with only 11·1% dogs that were still in remission at 6 months, later going on to have a relapse. Since most relapses were easily managed, the benefit of continuing lifelong immunosuppressive medications in all dogs to prevent relapse in this small cohort is questionable.

Although discontinuation of medications did not appear to be associated with relapse, certain disease factors during hospitalisation

did appear to be associated with an increased incidence of later relapse. Most interestingly, there was a significantly higher incidence of relapse in animals that had received a blood transfusion during their initial hospitalisation. This is unlikely to be a direct effect of the transfusion since most of these relapses occurred at least 2 months after hospitalisation. However, it is possible that the need for blood transfusion is an indicator of disease severity. A previous study showed that dogs with melaena had an increased need for blood transfusions, and that melaena was associated with a poorer prognosis (O'Marra *et al*. 2011). It is possible that the patients requiring transfusion in this study had more severe disease, and that patients with more severe disease are also at increased risk of relapse later throughout the course of treatment. In this study, the incidence of melaena was not significantly different between relapsing and non-relapsing dogs. However, the time for recovery of platelets was significantly longer in the dogs that relapsed, providing some support to the hypothesis that dogs with more severe disease at the time of hospitalisation are more likely to be at risk for complications long term.

The limitation of this study was that it was retrospective in nature, and therefore the treatment protocols and follow-up intervals were not standardised. The tapering and discontinuation of medications were at the discretion of the attending clinician and may have been influenced by individual clinician bias – anecdotally in our hospital, some clinicians are more likely to discontinue medications in stable patients than others – as well as patient factors. Ultimately, there was not enough information provided from the records to determine the rapidity of the tapering of medications or frequency or recheck examinations, which may have influenced relapse. To more thoroughly investigate the possible influence of long-term medications on the incidence of relapse would require a prospective study with medications being discontinued at random after a set time period in a proportion of the dogs.

We initially set very broad inclusion criteria for the study requiring only that a platelet count was less 150×10^9/L, a minimum of *Ehrlichia canis* and *Anaplasma phagocytophilum* testing, and abdominal imaging. Previous studies have shown that the majority of primary immune-mediated thrombocytopenia dogs will present with a platelet count of less than 30×10^9/L (Putsche & Kohn 2008). Indeed, although our inclusion criteria was set at 150×10^9/L all of the dogs in this study presented with platelet counts of less than 40×10^9/L, with the mean platelet counts being 10 x 10^9/L for the relapsing group and 19×10^9/L for the non-relapsing group. Thoracic imaging, pathologist review of blood smears, coagulation testing and extensive infectious disease testing were not required to be included in the study and it is possible that some patients may have had thrombocytopenia secondary to other underlying disease. However, in most patients a more complete evaluation for underlying causes of thrombocytopenia was performed and none was found in any case included in this study.

In conclusion, this study found a relapse rate of 31% in presumed primary immune-mediated thrombocytopenia with relapses occurring a median of 79 days after diagnosis. Most relapses occurred while patients were still receiving medications; and 50% of dogs that relapsed had at least one further relapse during the follow-up period. No benefit was apparent in continuing treatment indefinitely. However, the results do suggest that certain patients with more severe disease on presentation might benefit from being more closely monitored during treatment and tapering of medication.

Conflict of interest

No conflicts of interest have been declared.

References

Balog, K., Huang, A. A., Sum, S. O., *et al*. (2013) A prospective randomized Clincial trial of vincristine versus human intravenous immunoglobulin for acute adjunctive Management of Presumptive Primary Immune-Mediated Thrombocytopenia in dogs. *Journal of Veterinary Internal Medicine* **27**, 536-541

Bianco, D., Armstrong, P. J. & Washabau, R. J. (2009) A prospective, randomized, double-blinded, placebo-controlled study of human intravenous immunoglobulin for the acute Management of Presumptive Primary Immune-Mediated Thrombocytopenia in dogs. *Journal of Veterinary Internal Medicine* **23**, 1071-1078

Botsch, V., Kuchenhoff, H., Hartmann, K., *et al*. (2009) Retrospective study of 871 dogs with thrombocytopenia. *Veterinary Record* **164**, 647-651

Cummings, F. O. & Rizzo, S. A. (2017) Treatment of presumptive primary immune-mediated thrombocytopenia with mycophenolate mofetil versus cyclosporine in dogs. *Journal of Small Animal Practice* **58**, 96-102

Jackson, M. L. & Kruth, S. A. (1985) Immune-mediated hemolytic anemia and thrombocytopenia in the dog: a retrospective study of 55 cases diagnosed from 1969 through 1983 at the Western College of Veterinary Medicine. *Canadian Veterinary Journal* **26**, 245-250

Jans, H. E., Armstrong, J. & Price, G. S. (1990) Therapy of immune-mediated thrombocytopenia. *Journal of Veterinary Internal Medicine* **4**, 4-7

Kristensen, A. T., Weiss, D. J., Klausner, J. S., *et al*. (1992) Detection of antiplatelet antibody with a platelet immunofluorescence assay. *Journal of Veterinary Internal Medicine* **8**, 36-39

Lewis, D. C. & Meyers, K. M. (1996) Canine idiopathic thrombocytopenic purpura. *Journal of Veterinary Internal Medicine* **10**, 207-218

Nakamura, R. K., Tompkins, E. & Bianco, D. (2012) Therapeutic options for immune-mediated thrombocytopenia. *Journal of Veterinary Emergency and Critical Care* **22**, 59-72

O'Marra, S. K., Delaforcade, A. M. & Shaw, S. P. (2011) Treatment and predictors of outcome in dogs with immune-mediated thrombocytopenia. *Journal of the American Veterinary Medical Association* **238**, 346-352

Putsche, J. C. & Kohn, B. (2008) Primary immune-mediated thrombocytopenia in 30 dogs (1997-2003). *Journal of the American Animal Hospital Association* **44**, 250-257

Rozanski, E. A., Callan, M. B., Hughes, D., *et al*. (2002) Comparison of platelet count recovery with use of vincristine and prednisone or prednisone alone for treatment for severe immune-mediated thrombocytopenia in dogs. *Journal of the American Veterinary Medical Association* **220**, 477-481

Scott, M. A., Kaiser, L., Davis, J. M., *et al*. (2001) Development of a sensitive immunoradiometric assay for detection of platelet surface-associated immunoglobulins in thrombocytopenic dogs. *American Journal of Veterinary Research* **63**, 124-136

Scuderi, M. A., Snead, E., Mehain, S., *et al*. (2016) Outcome based on treatment protocol in patients with primary canine immune-mediated thrombocytopenia: 46 cases (2000-2013). *Canadian Veterinary Journal* **57**, 514-518

Wilkerson, M. J., Shuman, W., Swist, S., *et al*. (2001) Platelet size, platelet surface-associated IgG, and reticulated platelets in dogs with immune-mediated thrombocytopenia. *Veterinary Clinical Pathology* **30**, 141-149

Williams, D. A. & Maggio-Price, L. (1984) Canine idiopathic thrombocytopenia: clinical observations and long-term follow up in 54 cases. *Journal of the American Veterinary Medical Association* **185**, 660-663