Treatment and predictors of outcome in dogs with immune-mediated thrombocytopenia

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Objective—To characterize the clinical course of disease and identify prognostic indicators for immune-mediated thrombocytopenia in dogs.

Design—Retrospective cohort study.

Animals—73 dogs treated for immune-mediated thrombocytopenia at the Foster Hospital for Small Animals at the Tufts Cummings School of Veterinary Medicine and the Tufts Veterinary Emergency Treatment and Specialties Hospital.

Procedures—Medical records from the period of January 2002 through June 2008 were reviewed to identify dogs with a diagnosis of immune-mediated thrombocytopenia. Data collected included signalment, clinical signs, results of initial diagnostic tests, treatment, complications, and survival duration.

Results—Dog ages ranged from 5 months to 15 years (median, 8.1 years). Cocker Spaniels were overrepresented, compared with their distribution in the entire hospital population during the same period. Sixty-one of the 73 (84%) dogs survived to discharge. Seven (11%) of those dogs were lost to follow-up. Five of the remaining 54 (9%) dogs had a relapse of the disease. The presence of melena or high BUN concentration at admission to the hospital was significantly correlated with a decreased probability of survival.

Conclusions and Clinical Relevance—Immune-mediated thrombocytopenia is a serious yet treatable disease, which may have a lower rate of recurrence than previously reported. The presence of melena or high BUN concentration in the study suggested a poor prognosis for affected dogs. (*J Am Vet Med Assoc* 2011;238:346–352)

Immune-mediated thrombocytopenia is a common cause of severe thrombocytopenia in dogs.[1] Immune-mediated platelet destruction can be primary with no underlying cause or secondary to drug administration, infection, neoplasia, or blood transfusion.[2] Anti-platelet antibodies adhere to platelet surface antigens, stimulating Fc receptor–mediated phagocytosis of the circulating platelets by macrophages. Immune-mediated thrombocytopenia can also originate at the level of megakaryocytes within the bone marrow as a result of anti-megakaryocyte antibodies.

Diagnosis of IMT is typically one of exclusion. Disseminated intravascular coagulation and platelet consumption or sequestration must be carefully ruled out as peripheral causes of non–immune-mediated disease, and primary bone marrow disease such as drug toxicosis, leukemia, and paraneoplastic conditions should be considered as differential diagnoses.

An increased risk of spontaneous hemorrhage can develop in dogs with IMT and platelet concentrations < 30,000 cells/μL[3]; however, hemorrhage is unpredictable in dogs with IMT.[4] In humans, death due to hemorrhage is rare in childhood- and adult-onset ITP. The rate of intracranial hemorrhage in children with acute ITP has been estimated at 0.2% to 1%,[5] whereas fatal hemorrhage in adults with chronic ITP reportedly ranges from 0.004 to 0.13 cases/patient-year at risk, depending on age of the patient.[6]

Other retrospective studies[3,7] of ITP in dogs have shown that females are more commonly affected than males. Overrepresented breeds include Cocker Spaniel, Miniature and Toy Poodle, and Sheepdog.[7,8] Reported short-term survival rates range from 74% to 97%, with recurrence rates between 26% and 58%.[3,7,9] Despite the information gained from the aforementioned studies, no prognostic indicators that can be easily measured at the time of initial diagnosis have been identified. The purpose of the study reported here was to characterize the clinical course of disease and identify prognostic indicators for IMT in dogs.

Abbreviations

ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
IMT	Immune-mediated thrombocytopenia
ITP	Idiopathic thrombocytopenia purpura
PSAIgG	Platelet surface–associated immunoglobulin G

Materials and Methods

Dogs—Records of all dogs examined at the Foster Hospital for Small Animals at the Tufts Cummings School

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of Veterinary Medicine and the Tufts Veterinary Emergency and Treatment Specialties hospital from January 2002 through September 2008 were reviewed to identify dogs with a diagnosis of IMT. Inclusion criteria consisted of a clinical diagnosis of IMT and a platelet concentration < 50,000 cells/µL. Exclusion criteria consisted of an incomplete medical record or concurrent immune-mediated hemolytic anemia (Evans syndrome), as evidenced by spherocytosis or positive results of an autoagglutination test; neoplasia; or non–platelet-derived coagulopathy (defined as a considerably prolonged prothrombin time or partial thromboplastin time).

Medical records review—Data collected included dog signalment, relevant clinical history, clinical signs of IMT, duration and cost of hospital stay, complications, whether a blood transfusion was performed, whether the dog survived to discharge from the hospital, and results of diagnostic imaging and histologic analysis, when available. Data on dog survival status and whether the disease recurred were obtained from the referring veterinarian or from direct contact with owners at follow-up. End points for defining survival included survival to discharge, natural death, or survival to the end of the study period.

Statistical analysis—Statistical calculations were made by use of a commercially available software program.[a] A χ^2 test was performed to compare survival to discharge (yes vs no) between dogs with and without specific signs of disease. For nonparametric data, Mann-Whitney and Kruskal-Wallis rank sum analyses were performed and Pearson correlation coefficients were calculated to measure associations between clinical signs at initial evaluation or diagnosis and transfusion requirements, days to platelet count recovery, days of hospitalization, and survival duration. A value of $P \leq 0.05$ was considered significant.

Results

Dogs—One hundred sixty records were identified, of which 73 met the criteria for inclusion in the study. Of the excluded records, 8 were missing and 12 were incomplete; the remaining 67 did not meet the inclusion criteria. Ages of dogs ranged from 5 months to 15 years (median, 8.1 years). Cocker Spaniel was the only breed overrepresented (n = 6), compared with the entire hospital population of Cocker Spaniels during that period ($P = 0.01$). Twenty-seven dogs were male, 23 of which were castrated, and 46 were female, 44 of which were spayed. This distribution did not differ significantly from that of the entire hospital population ($P = 0.08$).

Clinical signs at initial evaluation—When first admitted to the hospital, 59 (81%) dogs had signs of bleeding (**Table 1**). The presence of melena at that time was significantly ($P = 0.03$) associated with failure to survive to discharge from the hospital. Of the 15 dogs that had melena, only 9 (60%) survived to discharge, whereas 52 of 58 (90%) dogs without melena survived to discharge. Dogs with melena at the time of admission were also more likely to require transfusion during hospitalization ($P = 0.02$). Twelve of the 15 (80%) melenic dogs required a blood transfusion, whereas only 15 of the 58 (26%) dogs without melena required transfusion. Platelet concentrations were similar in dogs with melena (median, 6,000 cells/µL; range, 2,000 to 29,000 cells/µL) and without melena (median, 5,000 cells/µL; range, 2,000 to 22,000 cells/µL).

Platelet concentrations were determined through use of an automated counter.[b] The median platelet concentration at hospital admission was 5,000 cells/µL (range, 1,000 to 29,000 cells/µL). Seven dogs had platelet concentrations that continued to decrease during the initial treatment period. The lowest recorded platelet concentration ranged from 1,000 to 24,000 cells/µL (median, 4,000 cells/µL). Initial platelet concentration and lowest recorded platelet concentration were not associated with survival to discharge ($P = 0.36$ and $P = 0.51$, respectively). All platelet concentrations were confirmed by evaluation of a blood film for platelet clumping and platelet estimation by trained laboratory personnel.

Twenty-six (36%) dogs had a high rectal temperature (> 39.2°C [102.5°F]) at the time of examination, ranging from 39.2° to 40.6°C (102.6° to 105.0°F). Twenty-seven (37%) dogs were anemic (PCV < 36%) at the time of hospital admission, with PCV ranging from 10% to 35%. Twelve (16%) dogs had a PCV < 25%. No relationship between PCV at hospital admission and survival to discharge was detected ($P = 0.14$).

Hematologic analysis—Hemograms as obtained via an automated counter[b] were available for 70 dogs.

Table 1—Association between evidence of clinical bleeding at the time of diagnosis and proportion surviving to hospital discharge in 73 dogs with IMT.

Nature of bleeding	No. of dogs affected	No. of affected dogs surviving to discharge	*P* value
Petechia or ecchymoses	48	37	0.24
Gingival bleeding	17	13	0.56
Melena	15	9	0.03
Hematemesis	14	10	0.29
Hematochezia	10	7	0.42
Epistaxis	11	8	0.43
Hematuria	10	9	0.45
Hyphema	8	7	0.93
Scleral hemorrhage	5	5	0.32

A value of $P \leq 0.05$ was considered significant. A significant value means that a greater proportion of dogs with the indicated type of bleeding failed to survive to discharge, compared with the proportion of dogs without that type of bleeding.

Twenty-two (31%) dogs had a high WBC concentration (ranges, 5,400 to 53,700 cells/µL; reference limits, 4,900 to 16,900 cells/µL). Twenty-eight (40%) dogs had an absolute neutrophilia (ranges, 3,240 to 41,234 cells/µL; reference limits, 3,000 to 13,000 cells/µL); none were neutropenic. Twelve (17%) dogs had evidence of a left shift (> 300 band cells/µL; range, 380 to 3,356 band cells/µL), and 7 (10%) dogs had slight to moderate toxic change evident in their neutrophils. Two (3%) dogs had a lymphocytosis (190 to 6,792 cells/µL; reference limit, < 5,000 cells/µL), and 12 (17%) dogs had reactive lymphocytes. Nineteen (27%) dogs had a monocytosis, ranging from 1,538 to 7,719 cells/µL (reference limit, < 1,500 cells/µL). Thirty (43%) dogs had nucleated RBCs ranging in count from 1 to 40/100 WBCs.

Prothrombin and activated partial thromboplastin time were measured in 39 dogs. No dogs had an increase > 10% higher than the upper reference limit in these values.

Serum biochemical analysis—Sixty-four dogs had a serum biochemical analysis performed (**Table 2**). In 14 (22%) dogs, BUN concentration was higher than the upper reference limit, and in 3 (5%) dogs, creatinine concentration was high. Six of the 14 dogs with a high BUN concentration did not survive to discharge from the hospital, compared with 6 of 41 dogs with a BUN within reference limits; this difference was significant ($P = 0.008$). Although 2 of the 3 dogs with a high creatinine concentration did not survive to discharge, this proportion did not differ significantly from that of dogs with a creatinine concentration within reference limits ($P = 0.08$).

Serum ALP activity was high in 25 dogs, ALT activity was high in 9 dogs, and hypoalbuminemia was evident in 19 dogs. These findings for ALP, ALT, and albumin had no association with whether a dog survived to discharge from the hospital ($P = 0.91$, $P = 0.16$, and $P = 0.09$, respectively). Serum ALT activity was remarkably high (ie, > 2× the upper reference limit) in 5 dogs, 4 of which survived to hospital discharge. The probability of death did not vary among these dogs ($P = 0.82$).

Bone marrow evaluation—Eleven dogs had bone marrow aspirates or biopsies performed, and specimens were histologically assessed. Seven of these dogs had signs of megakaryocytic hyperplasia, and 4 had absolute or relative megakaryocytic hypoplasia. Three of the 4 dogs with megakaryocytic hypoplasia and 6 of the 7 dogs with megakaryocytic hyperplasia survived to discharge from the hospital. Dogs with an active megakaryocytic line were no more likely to survive than were those without one ($P = 0.66$). Furthermore, the number of days until the platelet concentration exceeded 40,000 cells/µL did not differ significantly ($P = 0.63$) between dogs with megakaryocytic hyperplasia (range, 5 to 12 days) and dogs with absolute or relative hypoplasia (range, 4 to 23 days). Dogs that underwent a bone marrow evaluation had a significantly ($P = 0.004$) longer time to platelet recovery (> 40,000 cells/µL) than did dogs that did not undergo the procedure. The proportion of dogs that survived to discharge from the hospital was similar between the 2 groups (82% and 84%, respectively).

Treatments—All dogs received corticosteroids including prednisone (n = 64), dexamethasone sodium phosphate (35), or prednisolone acetate (8) during hospitalization, except for 1 patient that was euthanized at the time of diagnosis and another patient that had evidence of pneumonia at the time of admission. The mean dose of prednisone was 2.74 mg/kg (1.25 mg/lb; range, 1 to 4.65 mg/kg [0.45 to 2.11 mg/lb]), PO, once a day; that for dexamethasone sodium phosphate was 0.35 mg/kg (0.16 mg/lb; range, 0.18 to 0.60 mg/kg [0.08 to 0.27 mg/lb]), IV, once a day, and mean dose of prednisolone acetate was 2.29 mg/kg (1.04 mg/lb; range, 1.08 to 3.69 mg/kg [0.49 to 1.68 mg/lb]), SC, once a day. The dog with pneumonia received only vincristine and azathioprine. Only 9 dogs received only corticosteroids. Vincristine and azathioprine were commonly used in conjunction with corticosteroids (**Table 3**). Results of χ^2 tests comparing the probability of survival to discharge for each combination of drugs with that of all other treatments revealed that a single dog that received combined treatment with corticosteroids, cyclosporine, vincristine, and mycophenolate mofetil had a significantly ($P = 0.02$) lower probability of survival to discharge than did dogs that received other immunosuppressive treatments.

Treatment with gastrointestinal protectants including famotidine, omeprazole, pantoprazole, and sucralfate was common: 62 of 73 (85%) dogs received one or more of these drugs. However, protectant treatment was not associated with the probability of surviving to hospital discharge ($P = 0.43$).

Fifty-seven dogs received doxycycline, although anti-rickettsial antibody titers were measured in only 41 dogs. Most dogs had an antibody titer panel reflecting the most common rickettsial infections in Massachusetts (Lyme disease [C_6 antibody], *Ehrlichia canis* infection, *Anaplasma phagocytophilum* infection, and Rocky Mountain spotted fever). Of those 41 dogs, 14 (34%) had positive results for Lyme C_6 antibody consistent with prior or current infection. Eight had antibody titers against *A phagocytophilum* that exceeded 1:80, and 4 had positive results for Rocky Mountain spot-

Table 2—Significance of associations of serum biochemical abnormalities with proportion surviving to hospital discharge in 73 dogs with IMT.

Abnormality	No. of dogs	Median (range)	Reference limits	*P* value
High BUN (mg/dL)	14	41.5 (33–93)	8–30	0.002
High creatinine (mg/dL)	3	4.0 (3.7–4.4)	0.6–2.0	0.08
Low albumin (mg/dL)	19	2.3 (1.6–2.7)	2.8–4.0	0.09
High ALP (U/L)	25	229 (130–2,353)	12–127	0.91
High ALT (U/L)	9	227 (93–720)	14–86	0.16

See Table 1 for key.

Table 3—Immunosuppressive and adjunctive treatments administered during hospitalization of dogs with IMT and survival rate.

Treatment	No. of dogs treated	No. of treated dogs surviving to discharge	*P* value*
CS	9	7	0.52
CS + Vinc	30	25	0.74
CS + Vinc + Aza	23	22	0.21
CS + Vinc + Cyclo	3	2	0.84
CS + Aza	2	2	0.57
CS + Aza + Cyclo	1	1	0.69
CS + Vinc + Aza + hIVIG	1	1	0.69
CS + Vinc + Cyclo + MM	1	0	0.02
Vinc + Aza	1	1	0.69

*P value is the result of χ^2 analysis comparing the proportion that survived to discharge in the indicated group with the proportion that survived to discharge in all other dogs.

Aza = Azathioprine. CS = Corticosteroid. Cyclo = Cyclosporine. hIVIG = Human IV immunoglobulin. MM = Mycophenolate mofetil. Vinc = Vincristine.

A value of $P \leq 0.05$ was considered significant. A significant value means that a greater proportion of dogs that received the indicated treatment failed to survive to discharge, compared with the proportion of dogs that did not receive that particular treatment or set of treatments.

ted fever (> 1:80). No dogs had antibody titers against *E canis* that exceeded 1:80. In 2 dogs, *A phagocytophilum* morulae were detected on a blood film; however, antibody titers were not measured. Many dogs had antibodies against > 1 rickettsial organism. In total, 18 of the 73 (25%) dogs had evidence of rickettsial infection.

Twenty-six (36%) dogs received a transfusion with whole blood or packed RBCs during hospitalization. Fourteen (19%) dogs required multiple transfusions, and the median number of transfusions in all dogs receiving transfusions was 2 (range, 1 to 10). Two dogs received fresh-frozen plasma in addition to RBC products, with the intention of preventing dilutional coagulopathy due to multiple transfusions.

Ultrasonography—Fifty-eight (79%) dogs underwent abdominal ultrasonography to detect evidence of underlying disease. Given the fact that dogs with evidence of neoplasia were excluded from the study, most dogs had nonspecific changes such as hepatosplenomegaly (n = 21). Seventeen (81%) of those dogs survived to discharge, but this factor did not influence that outcome ($P = 0.58$). Because of the risk of hemorrhage, fine-needle aspirates were not performed in the study dogs.

Surgery—Two dogs underwent splenectomy during initial hospitalization. One dog had a remarkably inhomogeneous spleen detected during abdominal ultrasonography, and that spleen was removed at the time of exploratory laparotomy to remove an obstructing foreign body in the distal portion of the jejunum the day after admission. After treatment restored its blood platelet concentration to a healthy value, the second dog underwent splenectomy to remove a large mass detected in the spleen during abdominal ultrasonography. Histologic evaluation of splenic tissue from the first dog revealed lymphoid hyperplasia and extramedullary hematopoiesis, whereas that of the second dog revealed lymphoid hyperplasia alone.

Hospitalization—Sixty-one of the 73 (84%) dogs survived to hospital discharge. Two dogs were euthanized at the time of diagnosis and were eliminated from the survival analysis. The median duration of hospitalization in the remaining 71 dogs was 4 days (range, 0 to 15 days). The median cost of hospitalization was $2,222 (range, $459 to $12,596). Among dogs that survived to discharge from the hospital, the median duration of hospitalization was 5 days (range, 0 to 14 days), whereas that for nonsurvivors was 3 days (range, 1 to 15 days; $P = 0.21$).

Complications during hospitalization—Sixteen (22%) dogs had complications during their hospitalization. Five (7%) developed neurologic dysfunction that manifested as vestibular signs, abnormal posture, and mentation changes. Neurologic signs were transient in 4 dogs; however, 1 dog was euthanized for persistent mentation changes. Four (5%) dogs developed respiratory distress attributed to pulmonary hemorrhage, pulmonary thromboembolism, or acute lung injury.

Two (3%) dogs developed new respiratory signs including cough, tachypnea, or dyspnea, with thoracic radiography revealing lobar pulmonary infiltrates that were consistent with aspiration pneumonia. On the basis of clinical signs, 2 other dogs received a diagnosis of suspected pancreatitis while hospitalized. Neither received azathioprine.

Two dogs developed leukopenia during the course of treatment. In 1 dog, this was attributed to effects of vincristine, which the dog had received 5 days prior to developing leukopenia. The same dog also received prednisone and azathioprine. The second dog developed leukopenia 23 days after initial diagnosis. The leukopenia was attributed to the effects of azathioprine in this dog, which had also received prednisone and vincristine.

One (1%) dog that developed cardiopulmonary arrest was successfully resuscitated, but owners elected euthanasia because of ongoing respiratory distress and suspected hemothorax. Two dogs had evidence of clinically important gastrointestinal hemorrhage, 1 developed hemoperitoneum, 1 developed mild pericardial effusion with no tamponade that spontaneously resolved, and 1 developed hemothorax followed by respiratory and cardiac arrest. One dog developed glaucoma secondary to hyphema. Two dogs developed urinary tract

infections, and 1 of these went on to develop urosepsis. Two dogs had evidence of catheter-associated phlebitis.

In addition to the 2 dogs with signs of pneumonia and 2 dogs with urinary tract infections, 1 dog had a subcutaneous abscess of the tibiotarsal joint at the time of initial evaluation. Initial platelet concentrations for those 5 dogs ranged from 1,000 to 24,000 cells/µL and did not differ significantly ($P = 0.88$) from concentrations for dogs without signs of infection. Similarly, the proportion of dogs surviving to hospital discharge (80%) and days until the platelet concentration exceeded 40,000 cells/µL (range, 3 to 11 days) did not differ significantly ($P = 0.83$ and $P = 0.57$, respectively) between dogs with and without signs of infection.

Outcome after hospital discharge—Two of the 61 (3%) dogs that survived to hospital discharge developed thromboembolic events approximately 1 and 2 weeks afterward. One dog developed acute onset ascites approximately 1 week after discharge. Abdominal ultrasonography revealed a thrombus in the portal vasculature that was not present on the initial ultrasonogram. Platelet concentration at that time was 183,000 cells/µL. The dog was treated with clopidogrel, and signs resolved over a 2-week period. A second dog developed signs of lethargy and malaise. Abdominal ultrasonography revealed a splenic thrombus. Platelet concentration at that time was 194,000 cells/µL. That dog was treated with ultra–low-dose aspirin (0.5 mg/kg [0.23 mg/lb], PO, q 24 h); however, it was lost to follow-up.

The period of long-term follow-up ranged from 126 to 2,170 days. Seven (11%) surviving dogs were lost to follow-up. Of the remaining 54 dogs, 5 (9%) had signs of relapse (ie, platelet concentration < 150,000 cells/µL) that were treated with resumption of immunosuppressive medications. Median interval to relapse was 1,743 days (range, 735 to 2,555 days). Thirty-five dogs were still alive at the end of the study period and were not included in median survival time.

Nineteen (26%) of all 73 dogs died at some point during the study period. The exact cause of death was not known for most dogs. Median interval until death by any cause after hospital discharge was 328 days (range, 10 to 2,164 days). Eight (11%) surviving dogs died within the first 6 months after discharge, and 46 (63%) dogs survived > 6 months after discharge. Of the 35 dogs still alive at the end of the study period, days since hospital discharge ranged from 265 to 1,619 days, with a median of 590 days.

The interval from initial diagnosis to complete weaning off all immunosuppressive medications was known for 19 dogs. The median interval to complete weaning was 123 days (range, 29 to 465 days). Additionally, 2 dogs were treated with azathioprine every other day until the time of death. Weaning information was available for only 1 dog that had a relapse of IMT. For that dog, all immunosuppressive treatment was stopped on day 123 after discharge from the hospital, and the relapse occurred 15 days later.

Discussion

In this study of prognostic indicators for IMT in dogs, 2 important factors were identified, both of which were noticed when the study dogs were admitted to the hospital. First, the presence of melena at the time of initial examination was associated with a lower probability of survival. In dogs with profound thrombocytopenia, melena most likely represents gastrointestinal mucosal bleeding secondary to thrombocytopenia. Dogs with melena also an had increased need for a blood transfusion relative to those without melena, which may translate into an increased cost of care and consequent euthanasia if owners cannot afford such care. Because the melena was present at the time of diagnosis, corticosteroid intolerance was not believed to have contributed to this phenomenon. It is possible that gastrointestinal mucosal bleeding of a great enough magnitude to cause frank melena may be a sign of endothelial dysfunction due to systemic inflammation, or it may be a manifestation of platelet dysfunction associated with antiplatelet antibodies, given that platelet concentrations were similar in dogs with and without melena.

The second indicator of a decreased probability of survival in dogs with IMT was the presence of a high BUN concentration at the time of hospital admission. Seven dogs, 4 of which survived, had both a high BUN concentration and melena, and this proportion of surviving dogs was similar to that for dogs with either melena or a high BUN concentration. A high BUN concentration can result from renal, prerenal (prior to production of urine), or postrenal (after production of urine) dysfunction.[10] No dogs with IMT in the study had postrenal dysfunction; however, it was difficult to determine whether azotemia was due to prerenal effects such as dehydration or gastrointestinal hemorrhage or was caused by concurrent renal dysfunction. Although dogs with a high BUN concentration appeared to have a lower PCV value than dogs without that abnormality, the difference was not significant ($P = 0.09$). Gastrointestinal hemorrhage likely played a role in the increase in BUN concentration. A high serum creatinine concentration (identified in 3 dogs) also appeared to be associated with failure to survive to hospital discharge, but again this association was not significant ($P = 0.08$). It may be that dehydration due to blood loss prior to hospital admission or concurrent renal disease was involved in the guarded prognosis in these dogs.

Similar to findings in another study,[11] there appeared to be more female than male dogs with IMT. On the other hand, age of onset of IMT (median, 8.1 years) was slightly older than previously reported (4 years[10] and 6 years[3,9,12]).The 4-day median interval to restoration of platelet concentrations to within reference limits was also comparable with previously reported values,[7,9,12] as was the 84% short-term survival rate.[3,9] In the dogs for which long-term follow-up information was available, the recurrence rate was only 9%, which was much lower than previous findings of 26% to 50%.[3,7,9] This lower rate may have reflected the inclusion of dogs with secondary IMT caused by rickettsial infection in the present study, as one would not expect affected dogs to have recrudescence of clinical signs with appropriate antimicrobial treatment. The lower survival rate might also have resulted from differences in study populations, initial treatment, or treatment weaning strategy.

Differentiating between primary and secondary IMT at the time of initial diagnosis is often difficult.

Initial positive results of serologic tests for rickettsial infections in endemic areas can be challenging to interpret because antibody titers may reflect prior exposure rather than active infection. For this reason, dogs believed to have an underlying rickettsial infection were included in the analysis of all dogs evaluated for IMT in our study.

Two dogs in the present study were returned to the hospital 1 to 2 weeks after discharge because of signs attributable to thrombus formation. Inflammation and coagulation are intimately connected.[13] The widespread inflammation and endothelial injury common to immune-mediated disease that might otherwise result in overt hypercoagulability could be lacking in dogs with IMT simply because of the paucity of platelet substrate on which to assemble the thrombin complex. Immune-mediated hemolytic anemia has a high risk of thrombosis.[14–16] It may be that a similar propensity toward hypercoagulability exists in IMT, but that this hypercoagulability is not expressed until platelet concentrations rebound to near-healthy ranges. Other possible causes of hypercoagulability and thrombus formation include effects of prednisone or the release of immature, easily activated platelets from the bone marrow.

Few dogs included in the present study underwent a bone marrow examination. Other researchers found that megakaryocytic hypoplasia is a poor prognostic indicator in dogs with idiopathic IMT.[3] Among the 11 dogs with bone marrow evaluation in our study, no significant difference in interval to platelet concentration recovery or in probability of surviving to hospital discharge was evident between dogs with and without megakaryocytic hypoplasia. The 11 dogs included those with the longest interval to platelet concentration recovery; for the most part, bone marrow examination was performed after treatment appeared to be failing. Consequently, these dogs do not represent the population as a whole, and the prevalence of megakaryocytic hypoplasia in our study should be interpreted with care. Failure to demonstrate prognostic value of the presence or absence of megakaryocytic hyperplasia may have been related to the dogs themselves or the timing of bone marrow sample collection. Ideally, diagnosis of IMT should include evaluation of the bone marrow early in the course of disease to rule out primary bone marrow disease; however, a recent study[17] in dogs revealed that bone marrow aspiration and cytologic analysis rarely result in a specific diagnosis in dogs with severe thrombocytopenia. Bone marrow evaluation is not recommended for humans < 60 years of age with suspected IMT.[18] In our study, clinician impression of bone marrow examination as a low-yield test may have influenced the decision to forego bone marrow evaluation in most dogs.

Testing for the presence of PSAIgG in blood can identify platelet-bound antibodies, supporting a clinical diagnosis of IMT. The PSAIgG assay is sensitive and specific for detecting platelet-bound antibodies; however, it does not discriminate between primary and secondary IMT, and positive results are possible in dogs with glomerulonephritis, neoplasia, hepatitis, or pancreatitis.[19] One negative aspect of the assay is that it is extremely sensitive to sample handling and storage.[20] Because of the lack of an on-site facility to perform the assay, the dogs in our study were not tested for PSAIgG.

Dogs with IMT often have considerable blood loss and develop changes associated with extramedullary hematopoiesis in the spleen and liver. Hypoxic insult to the liver caused by anemia can also result in regenerative nodules. In our study, abdominal ultrasonography was performed several days after initiation of corticosteroid therapy, and therefore, any hepatic changes detected may have been consistent with early steroid hepatopathy. Because of the risk of hemorrhage in dogs with severe thrombocytopenia, fine-needle aspiration of the spleen or liver is rarely performed. No evidence of lymphoma or other neoplastic processes was identified in the 19 study dogs with ultrasonographic evidence of hepatosplenomegaly for which long-term follow-up was available, although infiltrative neoplasia such as lymphoma could not be ruled out in these dogs.

Treatment of IMT is aimed at immunosuppression, most commonly with glucocorticoids. Other immunosuppressive drugs such as azathioprine or cyclosporine are commonly used in conjunction with glucocorticoids. Vincristine is often administered to facilitate release of platelets from the bone marrow.[21] In 1 study,[21] administration of vincristine in addition to prednisone shortened the interval to platelet concentration recovery relative to that of prednisone alone. Recently, IV administration of immunoglobulin has garnered attention as an adjunctive immunosuppressive treatment in humans that can be used in the short term to reduce the interval to platelet concentration recovery.[22] Comparison of survival rates among dogs stratified by treatment combinations revealed a significant difference (ie, lower probability of survival) in only 1 dog that received a corticosteroid, vincristine, cyclosporine, and mycophenolate mofetil. However, because only 1 dog received this treatment combination, one is prevented from drawing any conclusions about the combination's effectiveness or lack thereof.

a. SPSS, SPSS Inc, Chicago, Ill.
b. CellDyne 3700, Abbott Laboratories, Abbot Park, Ill.

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