
Michael D. Lucroy, DVM, MS, DACVIM, and Bruce R. Madewell, VMD, MS, DACVIM

Objective—To describe diseases, prognosis, and clinical outcomes associated with extreme neutrophilic leukocytosis in cats.

Design—Retrospective study.

Animals—104 cats with extreme neutrophilic leukocytosis.

Procedure—Medical records from 1991 to 1999 were examined to identify cats that had ≥50,000 WBC/µl with ≥50% neutrophils. Signalment, absolute and differential WBC counts, rectal temperature, clinical or pathologic diagnosis, duration and cost of hospitalization, and survival time were reviewed.

Results—Mean age of cats was 8.3 years, mean WBC count was 73,055 cells/µl, and mean absolute neutrophil count was 59,046 cells/µl. Mean duration of hospitalization was 5.9 days, and mean cost of hospitalization was $2,010. Twenty-nine (28%) cats were febrile, and 63 (61%) cats died. Overall median survival time was 30 days. Cats with neoplasia were nearly 14 times as likely to die unexpectedly as cats with other diseases.

Conclusions and Clinical Relevance—Extreme neutrophilic leukocytosis was associated with a high mortality rate. The prognostic importance of extreme neutrophilic leukocytosis should not be overlooked. Cats and dogs have similar diseases, mortality rates, and treatment costs associated with extreme neutrophilic leukocytosis. (J Am vet Med Assoc 2001;218:736–738)

More than 100 years ago, it was observed that blood leukocyte counts increase after administration of foreign proteins and bacterial products. In the late 1940s, the leukocyte response to inflammation or infection was recognized in humans. In a report of humans with extreme neutrophilic leukocytosis, the majority of patients did not have associated infection but did have an increased risk of mortality. Similarly, dogs with leukocytosis and neutrophilia without concurrent infection have high mortality rates.

In cats, pronounced leukocytosis and neutrophilia may accompany local or systemic infection, immune-mediated disease, tissue necrosis, neoplasia, or myeloid leukemia. Although veterinarians are familiar with causes for neutrophilic leukocytosis, there are few reports in the veterinary literature that describe the incidence of specific diseases in cats with extreme neutrophilic leukocytosis. Likewise, the morbid or lethal significance of extreme neutrophilic leukocytosis in cats has not been well-characterized.

The purposes of the study reported here were to describe the diseases, prognosis, and clinical outcomes associated with extreme neutrophilic leukocytosis in cats, and to compare these results with findings reported in dogs.

Criteria for Selection of Cases

Medical records from cats examined at the University of California Veterinary Medical Teaching Hospital (UCDVMTH) between February 1991 and November 1999 were examined for evidence of extreme neutrophilic leukocytosis, defined as WBC count ≥50,000 cells/µl, with neutrophils comprising ≥50% of the leukocytes. Reference ranges used by the UCD-VMTH hematology laboratory were based on mean values derived from a population of healthy adult cats. The reference range for total WBC count is 5,000 to 15,000 cells/µl, the reference range for absolute neutrophil count is 2,500 to 11,300 cells/µl.

Procedures

Data derived from medical records included age, breed, sex, date of hemogram indicating extreme neutrophilic leukocytosis, body temperature concurrent with the hemogram, temporally associated clinical or pathologic diagnoses, duration of hospitalization, and clinical outcome (mortality rate and survival time). Hospitalization costs were determined for only those cats hospitalized between January 1996 and November 1999. On the basis of clinical data, results of laboratory tests, and interpretation of pathologic findings, a cause for leukocytosis was determined for each cat and classified as infection, tissue necrosis, immune-mediated disease, neoplasia (excluding leukemia), or leukemia. Duration of hospitalization and survival times were calculated from the time of the first hemogram in which extreme neutrophilic leukocytosis was detected until discharge from the hospital or death of the patient.

Quantitative data (mean ± SEM, unless otherwise stated) were compared among disease categories by use of 1-way ANOVA, and the Tukey multiple comparisons test was used to determine which means were significantly different. Estimated survival curves were generated using the method of Kaplan and Meier, and compared by use of the log-rank test. Risk factors for mortality were identified by the odds ratio. All statistical tests were performed by use of commercially available software. Values of P < 0.05 were considered significant.

From the Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of California, Davis, CA 95616. Dr. Lucroy’s present address is the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK 74078.

The authors thank Raymond Cabral for technical assistance. Address correspondence to Dr. Madewell.
Results

One hundred nine cats that had total WBC > 50,000/µl were identified. Five of these cats were excluded from the study, however, because neutrophils comprised < 50% of the WBC count. Cats excluded because of insufficient neutrophilia included those with acute myelogenous leukemia (n = 1), idiopathic hyperesinophilic syndrome (1), and lymphoma (3).

The remaining 104 cats were included in the study. Breed distribution of this population included domestic shorthair (n = 58), domestic longhair (20), Siamese (9), domestic medium hair (5), Manx (4), Abyssinian (3), Persian (3), and 1 each of Burmese and Himalayan. There were 53 male cats (5 sexually intact, 48 neutered) and 51 female cats (9 sexually intact, 42 neutered). The male-to-female ratio was 1.04. Mean age (n = 102) was 8.2 ± 0.47 years (range, 1 month to 19 years). Mean body weight (n = 93) was 3.7 ± 0.12 kg (8.1 ± 0.26 lb; range, 1.2 to 8.2 kg [2.6 to 18.0 lb]). Mean age and body weight were not significantly different among disease categories. Of the 104 cats studied, 8 were from a single household.

Mean WBC was 73,055 ± 5,092 cells/µl (range, 50,400 to 458,000 cells/µl). Mean absolute neutrophil count was 59,046 ± 4,281 cells/µl (range, 25,200 to 370,770 cells/µl). Significant differences were not detected in mean WBC count or absolute neutrophil count among disease categories.

Sixty-eight (65%) cats were hospitalized; the remaining cats were outpatients. Mean duration of hospitalization was 3.9 ± 0.72 days (range, 2 to 34 days). Mean duration of hospitalization was shorter for cats with neoplasia (mean, 3.6 ± 1.1 days) and longer for cats with tissue necrosis (mean, 8.9 ± 3.0 days); however, differences were not significant. Mean cost of hospitalization was $2,010 ± $353 (range, $125 to $12,616; n = 53). Mean cost of hospitalization did not differ significantly among the disease categories.

Thirty-eight (37%) cats had infections (pyothorax [n = 7]; abscess [5]; pyelonephritis [4]; enteritis [4]; FeLV [4]; septic peritonitis [3]; septicemia [2]; feline immunodeficiency virus [1]; pneumonia [1]; pyometra [1]; feline infectious peritonitis [1]; cholangiohepatitis [1]; septic arthritis [1]; upper respiratory infection [1]; urinary tract infection [1]; and infection with Hemobartonella spp [1]). Twenty-three (22%) cats had immune-mediated disease (immune-mediated hemolytic anemia [n = 9]; glomerulonephritis [6]; vasculitis [4]; A/B transfusion reaction [1]; renal transplant rejection [1]; immune-mediated hemolytic anemia with immune-mediated thrombocytopenia [1]; and systemic lupus erythematosus [1]). Twenty-four (23%) cats had neoplasia (lymphoma [n = 11]; mast cell tumor [3]; oral squamous cell carcinoma [1]; metastatic poorly differentiated carcinoma [1]; mammary carcinoma [1]; bronchogenic carcinoma [1]; hemangiosarcoma [1]; histiocytic sarcoma [1]; pancreatic carcinoma [1]; leiomyosarcoma [1]; hepatocellular carcinoma [1]; and intra-abdominal mass [1]). Nineteen (18%) cats had tissue necrosis (induced by trauma [n = 3]; pancreatitis [5]; thrombosis [2]; intestinal foreign body [1]; necrotizing dermatitis [1]; steatitis [1]; uremic pneumonitis [1]; necrotic digit [1]; myonecrosis [1]; and necrotizing enteritis [1]). No cases of leukemia were identified.

Twenty-nine (28%) cats were febrile (body temperature ≥ 39.1 C [102.5 F]) at the time of extreme neutrophilic leukocytosis (x axis = survival time in days; y axis = proportion of cats surviving). Cats with concurrent infection (middle; solid line, n = 38) had significantly (P = 0.003) longer survival times than cats without concurrent infection (dashed line, 65). Male cats (bottom; solid line, n = 52) had significantly (P = 0.046) longer survival times than female cats (dashed line, 51).
Neutrophilic leukocytosis is encountered often in clinical practice, and veterinarians are typically well-acquainted with the underlying causes. However, there have been few descriptions in the veterinary literature of the morbid or lethal consequences of high leukocyte counts. A high mortality rate has been associated with neutrophilic leukocytosis. Thirteen (12%) cats died from unrelated causes. A significant difference was not detected in mean absolute neutrophil count or WBC count between cats that lived and those that died. One cat was lost to follow-up and was excluded from survival analysis. Overall median survival time for the remaining cats (n = 103) was 30 days. Significant differences were not detected among median survival times for cats with neoplasia (13 days), tissue necrosis (16 days), and immune-mediated diseases (8 days). However, median survival time of cats with concurrent infection (270 days) was significantly (P = 0.003) longer than for other groups. Median survival time of male cats (42 days) was significantly (P = 0.046) longer than for female cats (13 days). Survival curves for all cats, cats with and without infection, and male and female cats were determined (Fig 1).

A significant association was detected between mortality and neoplasia (odds ratio, 13.64; P = 0.001). The remaining variables, including sex, neuter status, tissue necrosis, infection, immune-mediated disease, breed, fever, hypothermia, and hospitalization were not associated with mortality.

Discussion

Neutrophilic leukocytosis is encountered often in clinical practice, and veterinarians are typically well-acquainted with the underlying causes. However, there have been few descriptions in the veterinary literature of the morbid or lethal consequences of high leukocyte counts. A high mortality rate has been associated with neutrophilic leukocytosis in humans, and similar observations have been made in dogs with leukocytosis and neutrophilia. Likewise, 61% of the cats described herein died suddenly because of the underlying disease process causing extreme neutrophilic leukocytosis. This is higher than the mortality rate (31%) reported for humans but is consistent with the mortality rate (62%) reported for dogs. This may be attributable, in part, to the effect of euthanasia on the mortality rate reported in veterinary studies, or the lower inclusion criteria (leukocytes > 25,000 cells/µl; neutrophils > 12,500 cells/µl) used in the study in humans. In the present study, we examined underlying diseases and clinical outcomes in cats with extreme neutrophilic leukocytosis, defined as ≥ 50,000 cells/µl with neutrophils ≥ 25,000 cells/µl. The selection of inclusion criteria for this study was somewhat arbitrary but reflected blood leukocyte counts that were > 3 times the upper limit of the hospital reference range. In cats, distinctions between stress leukon, leukemoid response, and extreme neutrophilic leukocytosis are unclear from descriptions in the veterinary literature. There are wide variations in published reference leukocyte values for healthy cats, depending, in part, on age and sex, with the highest mean values described in young (1 to 7 years) female cats (19,900 cells/µl) and adult (> 7 years) male cats (17,600 cells/µl). It is described in 1 textbook that a WBC count of 15,000 to 25,000 cells/µl is a stress leukon, a WBC count > 75,000 cells/µl is a leukemoid response, and a WBC count > 100,000 cells/µl is reason for concern. However, results from this study and our previous study in dogs indicate that much lower leukocyte counts are cause for concern. Because the association between extreme leukocytosis and morbidity or mortality is well-established in humans, many hospitals require the clinical laboratory to directly contact the clinician if the WBC count in a patient exceeds 25,000 cells/µl. It would be prudent for veterinary clinicians to consider more exact definitions for the terms stress leukon, leukemoid response, and extreme neutrophilic leukocytosis in cats.

In a previous report from our hospital of a similar study in dogs, a 2-year period was used to accrue approximately 100 cases that fit our criterion for inclusion. In the present study, an 8-year period was used to accrue a similar number of cases. This may be reflective, in part, of the hospital population, which has 3 times the number of dogs as cats, but conceivably reflects that cats with neutrophilic leukocytosis are less likely to respond to inflammatory stimuli, compared with dogs. Mean WBC count (73,055 cells/µl) in the cats of this study was greater, however, than mean WBC count (65,795 cells/µl) in dogs examined in a similar study, which indicates that the bone marrow will generate a strong leukemoid response to inflammatory stimuli in cats.

Causes for neutrophilic leukocytosis in cats were similar to those described in dogs. Nearly identical percentages of cats and dogs had neoplastic causes (23 and 20%, respectively) of neutrophilia and leukocytosis. Infectious causes were more common in cats than dogs (37 and 32%, respectively). A lower percentage of cats had immune-mediated causes than dogs (22 and 34%, respectively), whereas a higher percentage of cats (18%) had tissue necrosis as a cause for neutrophilic leukocytosis, compared with dogs (12%). These differences may be related, at least in part, to the often obscured distinction between disease categories and concurrent medical problems.

Cats with neoplasia as the underlying cause of extreme neutrophilic leukocytosis were more likely to die than cats with other diseases. This finding is similar to that reported for dogs. In contrast, there was no diminished mortality risk for hospitalized cats or cats with infections, as described in dogs. To reflect contemporary fees at the UCD-VMTH and to facilitate comparison with our previous study in dogs, records from a subset of cats examined between 1996 and 1999 were used for determination of mean costs associated with hospitalization. Mean cost for hospitalizing cats...
with neutrophilic leukocytosis was comparable to that for dogs ($2,010 and $2,028, respectively) despite a shorter duration of hospitalization (5.9 vs 7.4 days, respectively).

Of the 104 cats studied, 8 were from a single household, a household known over the past decade for introducing new cats into the household and housing large numbers of cats with persistent medical problems. Affected cats from this household spanned all 8 years of the study period. The diseases underlying neutrophilic leukocytosis in these 8 cats reflected infections, immune-mediated diseases, and cancer; the 1 common feature was FeLV infection. Seven of these 8 cats had been tested for FeLV, and results were positive in 5 of 7 cats.

That extreme neutrophilic leukocytosis accompanies such a plethora of underlying diseases should not be surprising given the > 50 chemokines and 14 chemokine receptors implicated in the production and mobilization of leukocytes. Because mature neutrophils are incapable of cell division, their sustained generation by bone marrow at high numbers (10^11 cells/d in clinically normal adult humans) is the result of a highly controlled, but incompletely understood, process of myelopoiesis.

Results of the study reported here revealed that various diseases are associated with extreme neutrophilic leukocytosis in cats. Clinicians should not disregard the prognostic importance of extreme neutrophilic leukocytosis in cats. Given that high mortality rates are associated with severe leukocytosis and neutrophilia in dogs and cats, a revision of the present veterinary definition of extreme leukocytosis may be warranted.

References