ABSTRACT

In cooperation with 15 practices in Florida, South Carolina, Tennessee, and Texas, data were collected on 215 cats with signs consistent with feline heartworm disease (FHD). Cats included in the study were over 6 months of age and presented with primary complaints of coughing or dyspnea, vomiting unrelated to eating, or acute death. Detailed signalment, thoracic radiographs, CBC, Knott or DIFIL® test, DiroCHEK® antigen test (Ag), and antibody (Ab) tests performed by Animal Diagnostics (AD) and Heska Corp (HC) were collected on each cat. Any cat that had positive antibody or antigen tests, and any cat with radiographic signs suggestive of FHD was scheduled for recheck examinations at 30 to 45 days and/or 60 to 90 days after initial presentation.

This study was designed to identify cats with concurrent or previous FHD, and to better characterize the presentation of this disease by following their progress. Of the 215 cats, 94 (44%) were Ab positive based on one or both tests. This indicated that the cat had been successfully infected with third-stage heartworm larvae and those larvae had developed to at least the fourth stage. Of the Ab-positive cats, 23/94 (24%) presented with vomiting; 39/94 (41%) presented with respiratory signs; and 27/94 (29%) had vomiting and respiratory signs.

Discordant results between the AD and HC antibody tests occurred, with the AD test detecting a higher number of antibody-positive cats. When comparing results of these Ab tests, no correlation was seen between the intensity of Ab level measured by the two tests, suggesting that different Ab is detected. One cat that died acutely with signs associated with FHD had relatively low Ab detected on both tests but had a positive DiroCHEK antigen test. No correlation between the level of antibody and the severity of clinical signs or radiographic pattern was found.

Eleven cats were DiroCHEK Ag positive on initial presentation. Of the Ag-positive cats, 2 were AD negative and 3 were HC negative. One cat was Ag positive and microfilaria positive but negative for Ab with both AD and HC tests. Although it has been presumed that most cats with FHD are Ag negative, it would appear that some individual cats with adult heartworms can also be Ab negative. Although eosinophilia and basophilia were more frequently associated with...
cats that were Ab positive, abnormal CBC values were observed in cats that were currently Ab negative. Radiographic lesions did not correlate with clinical signs or Ab levels. Some cats with no radiographic signs of FHD were Ag positive. Further, some cats with typical radiographic lesions of FHD were negative based on all serologic evaluations.

These results demonstrate that successful transmission of heartworms to cats is more common than previously thought and is clinically associated with coughing, dyspnea, and vomiting. A cause and effect correlation cannot be proven between clinical signs and laboratory evaluation. Radiographic evidence of FHD in cats with repeated negative antibody results may be an indicator of residual damage from previous heartworm infections. Most experimental studies of FHD have been short term (<1 yr). However, in this study, many cats underwent repeated clinical evaluation over a relatively short time. This demonstrated that the clinical picture of spontaneous FHD is a constantly changing syndrome, highly dependent on the stage (immature L₅, adult, adult death, residual damage) of the parasite in the cat and the individual cat’s response. On evaluation of clinically affected cats, no one test proved to be definitive (without exceptions). The diagnosis of FHD continues to require a combination of clinical evaluation and a series of diagnostic tests, often requiring reevaluations over time.

INTRODUCTION

Although many studies have classified the initial clinical presentation of heartworm-infected cats, a large-scale evaluation of cats with signs consistent with feline heartworm disease (FHD) over a period of several months in a clinical setting has not been reported. Long-term studies of experimental infections are uncommon. One objective of the study described here was to identify cats with concurrent or previous FHD, and to better characterize the clinical presentation of the disease by following their progress over several months period of time.

MATERIALS AND METHODS

As described in an overview of this study, 15 private veterinary practices in Florida, South Carolina, Tennessee, and Texas contributed cases to this study. Data were collected on 215 cats with signs consistent with FHD. Criteria for inclusion in the study were that cats must be more than 6 months of age and must be presented with primary complaints of chronic or intermittent coughing or dyspnea, or a pattern of intermittent vomiting unrelated to eating, or acute death of unknown cause. Each cat received a physical examination by the contributing veterinarian and a thorough history was taken. Each cat was evaluated by thoracic radiographs, complete blood count, Knott or DIFIL® (Evco) test for circulating microfilaria of Dirofilaria immitis, DiroCHEK® Canine Heartworm Antigen Test (Ag), and antibody (Ab) tests performed by Animal Diagnostics (proprietary laboratory test) and Heska Corporation (Heska™ Diagnostic Lab Feline Heartworm Test). Radiographs were given an overall score by the radiologist to reflect how strongly the findings were suggestive of feline heartworm disease. Scores were assigned as follows:

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no findings consistent with FHD</td>
</tr>
<tr>
<td>0.5</td>
<td>bronchointerstitial pattern, consistent with FHD, but nonspecific</td>
</tr>
<tr>
<td>1, 2, 3</td>
<td>increasing degrees of pulmonary artery enlargement, suggestive of FHD</td>
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As much data as possible were collected from cats that died acutely.

Any cat that had positive Ab, and any cat...
with radiographic signs suggestive of FHD was scheduled for recheck examinations at 30 to 45 days and/or 60 to 90 days after initial presentation. For any cat that died suddenly, the heart and lungs were fixed and submitted to Auburn University for further histopathologic examination.

**RESULTS**

Of the 215 cats presented, 94 (44%) were positive on one or both Ab tests. This indicated that the cat had been successfully infected with third stage heartworm larvae and those larvae had successfully molted to at least the fourth stage. Of the Ab-positive cats, 28% presented with dyspnea, 31% with coughing, 24% with vomiting, and 20% had both vomiting and coughing (Figure 1). Of the Ab-negative cats, 25% were presented with dyspnea only, 36% with coughing only, 21% with vomiting only, and 21% had both vomiting and coughing.

**Antibody Tests**

At the initial examination, 85 of the 215 cats (39.5%) evaluated with the Animal Diagnostics’ Ab test were positive, while 28 of the 212 cats (13.2%) tested with the Heska Ab test were positive. Discordance between these tests was evident, such that only 19 of the 85 cats positive by the Animal Diagnostics’ Ab test were also positive by the Heska Ab test. Of the 28 cats testing positive by the Heska Ab test, 19 were positive by the Animal Diagnostics’ test. This disparity between tests did not correspond to the degree of positivity on the descriptive scales used by either test.

For both tests, changes in the Ab status during the 3 examinations occurred with some cats. Some positive cats became negative, and some negative cats became positive. Of the cats which were positive by Animal Diagnostics’ test, 66% remained positive at all subsequent evaluations. Conversion from positive to negative or negative to positive on rechecks was more common using the Heska test.

**Antigen and Antibody Tests**

At the initial examination, 11 cats were Ag positive by the DiroCHEK test. As required in the protocol, these positive tests were confirmed by a second test. Of these 11 Ag-positive cats, 1 was negative by the Animal Diagnostics’ Ab test, and 3 were negative by the Heska Ab test. Only 8 of the cats were positive on both Ab tests at the initial examination. Two cats that were Ag negative at the initial evaluation were Ag positive at the second evaluation.

**Radiographs and Serology**

Ten of the 11 cats Ag positive at the initial examination were radiographed. Five of these (50%) scored 1, 2, or 3 on the radiograph score, 1 (10%) scored 0.5 and 4 (40%) scored 0. Conversely, the two cats that converted from Ag negative to positive at the recheck examination were initially considered FHD positive due to radiograph score of 1 in each case. Radiographic scores were somewhat higher in cats with marked elevations in Heska Ab test findings. In general, changes in radiographic scores on rechecks did not correlate with Ag or Ab results.


**Hematology**

Of the Ab-positive cats, 63% presented with peripheral eosinophilia and 10% with basophilia, but these findings were similar to those in Ab-negative cats, with 54% eosinophilia and 9% basophilia. In cats presenting with coughing, vomiting, or dyspnea, eosinophilia was a common finding, regardless of heartworm status or radiographic pattern of disease (Figure 2).

**Other Pets**

The majority of Ab-positive cats lived in households with other cats or dogs. The percentage of dogs on heartworm preventive was higher for the Ab-positive cats than for the Ab-negative cats. Of the Ab positive cats, 43% lived in households with other dogs and 68% lived in households with other cats. Comparing Ab-positive to Ab-negative cats living in households with dogs, 78% of the dogs living with Ab-positive cats were on heartworm preventive medications compared to 66% of the dogs living with Ab negative cats. The heartworm status of dogs was not determined (Figure 3).

**Lifestyle**

Of the total population of cats sampled, 87 (40%) of the cats lived entirely indoors and an additional 11% of the cats lived at least 90% of their time indoors, as classified by their owners. Of the cats testing positive by the Ag test, 9% were 100% indoor cats and 9% were 100% outdoor cats. Of the cats testing positive on Animal Diagnostics’ Ab test, 21% were 100% indoor cats and 12% were 100% outdoor cats. Of the cats testing positive on Heska Ab test, 18% were 100% indoor cats and 14% were 100% outdoor cats.

**Deaths**

One of the cats that died acutely was Ag positive and had one male and one female heartworm in the right heart and pulmonary artery, but this cat had only marginal Ab levels (70 by the Animal Diagnostics’ test and 10 by the Heska test).

**DISCUSSION**

These data reflect the different diagnostic pattern of this disease as dictated by the stage of the infection at presentation. Cats presented early in the disease process often have a diffuse alveolar pattern typical of allergic lung disease, but minimal pulmonary arterial changes visible on radiograph are Ag negative, and Ab positive. However, if presented late in the disease process, the cat may be both Ag and Ab positive and is more likely to have significant radio-
graphic pattern of pulmonary arterial disease.\textsuperscript{5,7,9,14,16} The interim stages of the disease have all the combinations, which have made the diagnosis of this disease challenging.\textsuperscript{12}

Discordant results between the two Ab tests occurred, with the Animal Diagnostics’ test detecting a higher number of Ab-positive cats. Other studies have demonstrated that these tests are quite specific for heartworm Ab.\textsuperscript{8} However, in this study, no correlation was seen between the intensity of Ab level measured by the two tests, suggesting that a different Ab is detected by each test and that the antigen producing the Ab in the Animal Diagnostics’ test is expressed earlier in the infection.\textsuperscript{8} Cats tend to become Ab positive earlier in the disease process with the Animal Diagnostics’ test, as compared to the Heska test.\textsuperscript{8} However, several cats found to be negative with the Animal Diagnostics’ test at initial presentation were positive with the Heska test. This change across time is significant in clinically reevaluating the cat over several months. One cat that died acutely with signs associated with FHD had relatively low Ab levels according to both tests but had a positive Ag test, and 2 worms were found in the heart on necropsy. Additionally, no correlation between the level of Ab and the severity of clinical signs, or radiographic pattern, was found, with the exception of some cats with highest levels by the Heska Ab test that had higher pulmonary arterial lesions scores. Cats presented for severe dyspnea did not appear to have higher Ab titers.

Throughout the course of the study, 13 cats were identified as Ag positive by the DiroCHEK test (11 of these at the initial evaluation). Two of these were negative for Ab on the Animal Diagnostics’ test and 3 were negative for Ab by the Heska test. One cat was Ag positive and microfilaria positive, but negative by both Ab tests. Cats with early fifth-stage larvae (early in the disease process), those with low worm burdens, immature worms, and/or male-only infections will be Ag negative on routine testing. Cats may present with clinical signs and radiographic lesions typical of early heartworm disease and be negative at the time of initial presentation, only to become positive on recheck by either Ab or Ag assays. Additionally, many cats may present as above and shift from heartworm positive to a negative status as the heartworms die spontaneously and the disease does not resolve. In a clinical setting, a negative Ab test usually rules out active heartworm disease, but the importance of rechecking at 30 to 45 days to check for conversion to Ab positive is reinforced by these data.

Radiographic lesions did not correlate with clinical signs or Ab levels. Some cats with no radiographic signs of FHD were Ag positive. Furthermore, some cats with radiographic lesions typical of FHD were negative based on all serologic evaluations. Two cats converted from Ag negative to Ag positive at the follow-up exam. Both of these cats also had radiographic signs suggestive of heartworm on initial examination. Cats with chronic radiographic signs of FHD, that are negative by serologic assays, could also reflect a previous infection. The pulmonary arterial lesions seen on radiographs have been well characterized in experimental studies.\textsuperscript{10,13} However, in cats with early L\textsubscript{5} infections, radiographically enlarged pulmonary arteries may not yet be evident,\textsuperscript{5} and the adult worms may not be visualized on echocardiographic examination.\textsuperscript{3,15}

Although eosinophilia and basophilia were more frequently associated with cats that were Ab positive, abnormal CBC values were also frequently observed in cats that were currently Ab negative and presented for respiratory signs or vomiting.

Most of the Ab-positive cats lived in households with other cats or dogs. Interestingly, the percentage of dogs on heartworm preventive was slightly higher in the Ab-positive cats than in the Ab-negative cats. There does not appear
to be any protective effect for cats living with dogs on heartworm preventive. This data demonstrate that these cats are still exposed to infective mosquitoes and are at risk of heartworm infection.

CONCLUSION

These results demonstrate that successful transmission of heartworms to cats showing signs of coughing, dyspnea, and vomiting is more common than previously thought. On evaluation of clinically affected cats, without exception, no one test proved to be definitive. Radiographic evidence of FHD in cats with repeated negative Ab results may be an indicator of residual damage from previous heartworm infections.

Most experimental studies of FHD have only investigated the first 6 to 8 months of heartworm infections using artificial infections with large numbers of infective third stage larvae. However, in this study, many cats underwent repeated clinical evaluation over a 2- to 3-month period after presentation of cats with clinical signs. Those cats that were confirmed positive demonstrated that the clinical picture of spontaneous FHD is a constantly changing syndrome, highly dependent on the stage (immature L₃, mature adult, adult death, residual damage) of the parasite in the cat and the individual cat’s response. The majority of cats with heartworm disease have minimal clinical signs after a mature heartworm infection develops. Although a negative Ab result has often been used to rule out heartworm disease, these data suggest that in some cases, cats with adult worms (as determined by microfilaria and Ag-positive results) can be Ab negative. Some cats with significant clinical disease associated with heartworm infections may not have changes in the pulmonary arteries on radiographic examinations. Neither the radiographic pattern nor intensity of Ab response should be used as a prognostic indicator for feline heartworm disease.

The diagnosis of FHD continues to require a combination of clinical evaluation and a panel of diagnostic tests, often requiring reevaluations over time. The traditional concept from canine heartworm disease, that adult worms cause disease and can usually be diagnosed with a single Ag test, does not apply to FHD. Disease in cats associated with early arrival of L₃, many of which die, has a different diagnostic profile than disease associated with death of adult heartworms. In this study, 44% of the cats presented with signs typically associated with heartworm disease were Ab positive, indicating that the cats had been successfully infected with L₃, which had lived 2 to 3 months and may or may not have developed into mature adult infections. Since different Ab tests are performed with different standards and methodologies, discordant results should not be unexpected and the different tests should be critically interpreted as they relate to stage of infection. The potential for abbreviated infections and chronic disease associated with past infections should be considered in the diagnostic approach of cats with respiratory signs, gastrointestinal signs, or acute death associated with signs suggestive of FHD.

ACKNOWLEDGMENT

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REFERENCES