Paragonimosis in a Cat and the Temporal Progression of Pulmonary Radiographic Lesions Following Treatment

Andrew S. Peregrine, BVMS, PhD, DVM, Stephanie G. Nykamp, DVM, Heather Carey, DVM*, Stephen Kruth, BA, DVM†

ABSTRACT

A 16 mo old cat presented with a 5 mo history of dyspnea, coughing, and gagging. Radiographic findings revealed seven nodules measuring 1–3 cm distributed multifocally in the lungs. Examination of feces revealed large numbers of eggs of *Paragonimus kellicotti*. Two fenbendazole treatment regimens (28 mg/kg *per os q* 12 hr for 21 days) and prednisone were required to eliminate the infection. Resolution of pulmonary nodules was monitored for 8 mo following successful treatment, and four lesions were still partially visible at 8 mo. (*J Am Anim Hosp Assoc* 2014; 50:356–360. DOI 10.5326/JAAHA-MS-6053)

Introduction

Within North America, the only trematode infection that is associated with pulmonary disease in cats is *Paragonimus kellicotti*.[1] Prevention of infection with that parasite is problematic because dogs, mink, bobcats, coyotes, foxes, goats, muskrats, opossums, raccoons, and skunks can also serve as definitive hosts.[2] However, of these various hosts, the mink (*Mustela vison*) is considered the primary definitive host.[3] Following development of patent infections in definitive hosts, eggs of *P. kellicotti* are shed in feces, and to a lesser extent, sputum. Thereafter, two intermediate hosts are required for the life cycle to continue: aquatic snails (*Pomatiopsis* spp.), then freshwater crayfish (*Cambarus* spp.). Cats and other definitive hosts become infected following ingestion of crayfish that contain metacercariae.[4]

Feline infections with *P. kellicotti* appear to be most common in the midwestern and southeastern regions of the US, in addition to the Great Lakes drainage region of the US and Canada.[1,5] Diagnosis of infection is carried out by examination of feces, sputum or tracheal wash for parasite eggs, and by radiography of the lungs. Radiographic features of feline pulmonary paragonimosis have been described in detail, and typically include poorly defined interstitial nodular densities and distinct pneumatocysts.[5,6] However, the duration of time it takes for the radiographic lesions to completely resolve following successful treatment, and thus their diagnostic specificity, has received limited attention. The cat described in this report had severe *P. kellicotti* radiographic lung lesions and was therefore examined on multiple occasions over a 316 day period following treatment to evaluate the persistence of radiographic lung lesions.

Case Report

A 16 mo old female domestic shorthair presented with a 5 mo history of dyspnea, coughing, and gagging. The cat had been adopted 7 mo earlier from a rescue in southern Ontario, and had been a stray before being taken in at that rescue. At the time of presentation (day 0), bouts of coughing typically occurred 20–30 times/day. The cat was eating and drinking normally and was normothermic. Auscultation of the thorax revealed lung sounds

From the Departments of Pathobiology (A.P.) and Clinical Studies (S.N., S.K.), Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada; and Tavistock Veterinarians, Tavistock, Ontario, Canada (H.C.).

Correspondence: aperegri@ovc.uoguelph.ca (A.P.)

CBC, complete blood count; SGFT, standard gravitational flotation technique; PO, *per os*

*H. Carey's present affiliation is Laurelwood Veterinary Hospital, Waterloo, Ontario, Canada.

†S. Kruth's present affiliation is Central Toronto Veterinary Referral Clinic, Toronto, Ontario, Canada.

that were mildly increased bilaterally. To determine whether there was an underlying immunosuppressive process, the cat was screened for feline leukemia virus and feline immunodeficiency virus[a] and tested negative for both pathogens. A complete blood cell count (CBC) performed on jugular blood[b] was unremarkable. Orthogonal thoracic radiographs revealed a pronounced diffuse bronchial lung pattern. Furthermore, seven nodules measuring 1–3 cm were distributed multifocally in the lungs (**Figures 1A, B**). One of the nodules was uniformly soft tissue in opacity (nodule 4 in Figure 1A) and six of the nodules had a soft tissue rim and were air filled (i.e., cavitated, pneumatocysts). Five of the seven nodules were located caudal to the heart. On the dorsoventral view (Figure 1B), the two cranial thoracic nodules (1 and 2) and one caudal lung lobe nodule (presumably nodule 7) were not visible. In contrast, nodule 4 was located in the left caudal lung field while nodules 3, 5, and 6 were located in the right caudal lung field. On the ventrodorsal view a small amount of fluid was noted in the left caudal thorax creating a thin pleural fissure line. Differential diagnoses for the focal solid and cavitated pulmonary nodules include parasitic granulomas (*P. kellicotti*, *Aelurostrongylus abstrusus*), neoplasia (e.g., bronchoalveolar carcinoma), abscesses (mycotic, bacterial [e.g., tuberculosis]), traumatic hematocysts, and, less likely, bronchial cysts.[6] In general, differential diagnoses for the diffuse bronchial lung pattern would include, in descending order of likelihood, allergic bronchitis, infectious bronchitis associated with a bacterial or parasitic infection, and neoplasia. Given the additional presence of pulmonary nodules in this case, either parasitic infection or neoplasia were considered most likely.

A fresh fecal sample from the cat was examined using a standard Baermann technique and failed to demonstrate the presence of nematode larvae.[7] As a result, infection with *A. abstrusus* was considered unlikely. The same fecal sample was examined with a standard gravitational flotation technique (SGFT), using saturated Na nitrate (specific gravity, 1.34), and demonstrated >100 eggs/g of feces of both *Paragonimus* sp. and *Ancylostoma* sp.[7] In light of the geographical location of the cat, those findings were considered indicative of infection with *P. kellicotti* and *Ancylostoma tubaeforme*.

To eliminate the *P. kellicotti* infection, the cat was treated with fenbendazole[c] (28 mg/kg *per os* [PO] *q* 12 hr for 21 days) beginning on day 0. In light of the extensive thoracic lesions, the cat was also administered prednisone[d] (0.6 mg/kg PO *q* 12 hr for 14 days then 0.6 mg/kg PO *q* 24 hr for 7 days). Treatment with prednisone began on day 3.

Eight days following initiation of therapy, the owner reported that the cat had made a substantive clinical improvement and had not coughed for at least 48 hr. However, on day 49 the cat was reportedly coughing as frequently as on day 0. Thoracic radiographs were therefore taken that day and, as before, indicated a diffuse bronchial lung pattern, but it was slightly improved compared with day 0 (**Figure 2**). The cavitated pulmonary nodules were smaller than on the initial study. The solid nodule (nodule 4) was unchanged in size but had become cavitated. A CBC examination of jugular blood collected on day 49 was unremarkable. However, examination of feces with SGFT indicated the presence of low numbers of *P. kellicotti* eggs. The cat was therefore treated a second time with the same fenbendazole and prednisone treatment regimens as before; both treatment

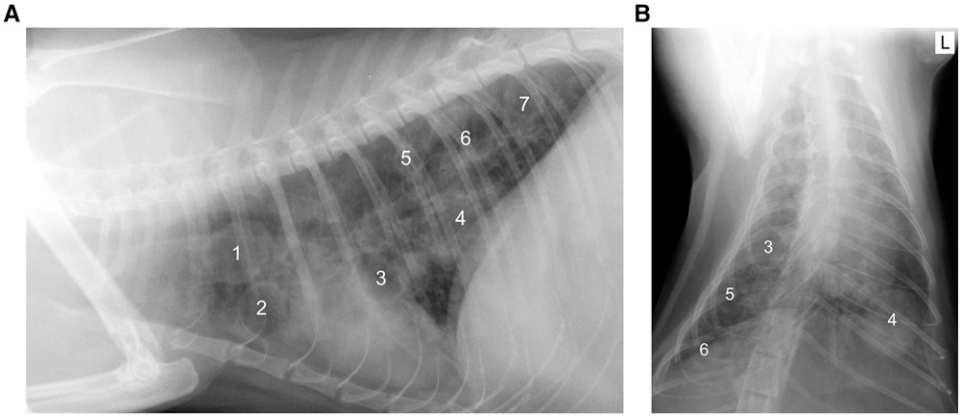

FIGURE 1 *Numbers represent the nodules as described throughout the text. Left lateral* (A) *and ventrodorsal* (B) *thoracic radiographs acquired on day 0 show a moderate diffuse bronchial pulmonary pattern with seven (six cavitated and one solid) focal pulmonary nodules. On the ventrodorsal view, a small amount of fluid is noted in the left caudal thorax. L, left lateral.*

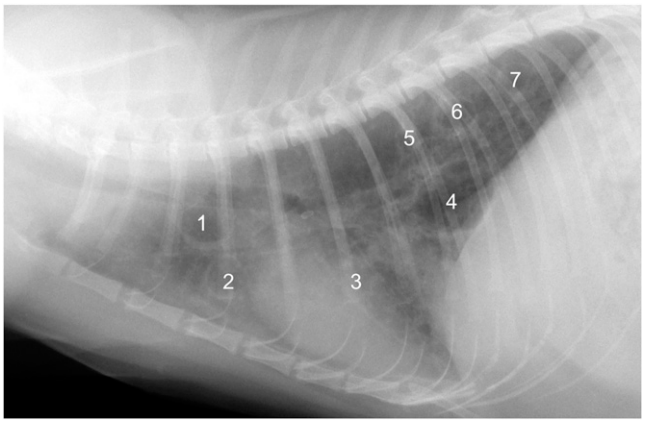

FIGURE 2 *Lateral thoracic radiograph taken on day 49 showing that all the pulmonary nodules are still evident but are decreased in size from the initial study (Figure 1). Nodule 4 is now cavitated compared with day 0.*

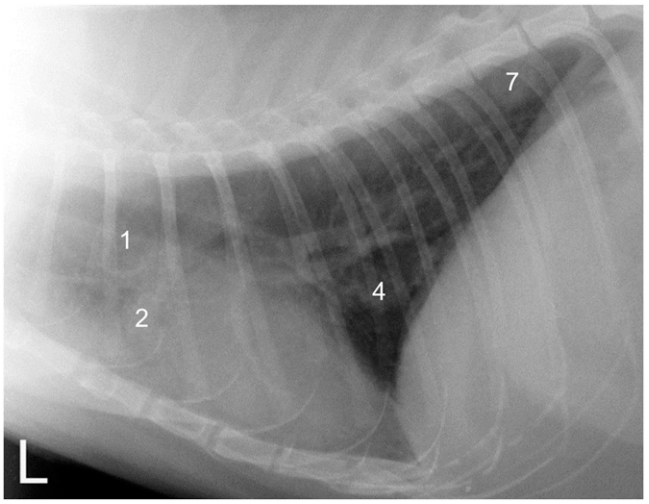

FIGURE 3 *A lateral thoracic radiograph taken on day 316 shows resolution of three of the seven nodules and a decrease in size in the remaining nodules.*

regimens began on day 58. On day 94, SGFT examination of feces was negative.

On day 135, the cat underwent a thorough clinical examination and was clinically normal. As before, CBC examination of jugular blood was unremarkable. As on day 94, parasite eggs were not detected when a fresh fecal sample was examined with the SGFT. A lateral thoracic radiograph performed that day showed that all nodules were still evident. Nodules 2–4 and 6 were all slightly reduced in size and nodules 1 and 5 were essentially unchanged. Nodule 7 was similar in size but had become more solid in appearance. The diffuse bronchial pattern was no longer present.

On day 221, the cat underwent a thorough clinical examination and again was considered clinically normal. As on day 135, a CBC examination of jugular blood and SGFT examination of feces were both unremarkable. Lateral thoracic radiography indicated that only five pulmonary nodules were now visible (1, 4–6, and 7), and all five lesions were less prominent than before.

On day 316, the cat underwent a final examination. As before, the cat was clinically normal and both CBC examination of jugular blood and SGFT examination of feces were unremarkable. Lateral thoracic radiography indicated that only four pulmonary nodules were visible (1, 2, 4, and 7) as shown in **Figure 3**. Nodules 1, 4, and 7 were markedly less prominent than on day 221. Nodule 7 remained solid in appearance, and nodule 2 had become more solid compared with day 135. It was unlikely that nodule 2 resolved on day 221 and then another lesion occurred in the same location on day 316. Most likely, variation in positioning resulted in the nodule being masked by a rib on day 221. A summary of the radiographic appearance of the pulmonary nodular lesions over the 316 day period following initial presentation and initiation of treatment is given in **Table 1**.

Discussion

Successful treatment of *P. kellicotti* infections in cats has previously been reported using albendazole at either 25 or 50 mg/kg PO *q* 12 hr for 14–21 days.[8,9] However, because both dosages of albendazole have been associated with side effects in cats, an alternative treatment option was requested for the case described herein.[8–10] Praziquantel (23 mg/kg PO *q* 8 hr for 3 days) has been shown to be efficacious.[11] However, in light of the bitter property of praziquantel when administered PO, this drug was not considered a practical therapeutic option. It was therefore decided to use fenbendazole (28 mg/kg PO *q* 12 hr for 21 days),

TABLE 1

Serial Evaluation of Thoracic Radiographic Nodules in a Cat Infected With *Paragonimus kellicotti* Following Initiation of Treatment With Fenbendazole on Day 0

	Thoracic Radiographic Nodule No.*							
Day	1	2	3	4	5	6	7	Total No. of Nodules Visible
0	C	C	C	S	C	C	C	7
49	C	C	S	C	C	C	C	7
135	C	C	S	C	C	C	S	7
221	C	—	—	(C)	C	C	S	5
316	C	S	—	(C)	—	—	S	4

*Refer to Figure 1A for nodule designation.
—, not visible; C, cavitated; (C), mild cavitation; S, solid and uniformly soft tissue in appearance.

which was previously shown to be efficacious against *P. kellicotti* infections in dogs.[12] That regimen was also predicted to eliminate the *A. tubaeforme* infection in the cat.[13] Examination of a fecal sample 28 days after completion of the first fenbendazole treatment regimen indicated that the cat was still shedding eggs of *P. kellicotti*. As a result, the cat was treated a second time with the same fenbendazole treatment protocol. Subsequently, multiple examinations of feces, beginning 16 days after completion of the second treatment, and improvements in both the clinical condition of the cat and radiographic appearance of the lungs over a 258 day period, indicated that the second treatment regimen eliminated the infection. Other studies indicated that cats stop shedding eggs in feces 6–10 days following initiation of effective treatment.[8,11] With respect to the diagnostic sensitivity of fecal examination methods, it should be noted that SGFT was used to examine fecal samples from the case described here. Although SGFTs have been used for diagnosis of *Paragonimus* infections in cats, sedimentation methods are generally considered more sensitive.[2,7,14–16] However, when the *Paragonimus* egg count is ≥350 eggs/g of feces, the diagnostic sensitivities of flotation and sedimentation techniques appear to be similar.[2]

In earlier work on the radiographic appearance of pulmonary paragonimosis in dogs and cats, focal lesions were considered to occur more commonly in the right lung than the left lung. In addition, caudal lung lobes were more often involved than cranial lobes, and middle and accessory lobes were least commonly affected.[6] The case described herein is consistent with those obervations. However, while formation of pneumatocysts appears to be normal with *P. kellicotti* infections in dogs, nodular interstitial densities appear to occur more commonly than pneumatocysts in cats.[6,9] In contrast, it should be noted that six of the seven focal radiographic lesions initially observed in the lungs of the cat described herein were pneumatocysts. Interestingly, other workers have noted a high frequency of pneumatocysts in cases of feline paragonimosis in central Canada.[14] It is possible that the difference in appearance of *P. kellicotti* lung lesions in cats in different parts of North America is associated with strains of parasite that differ in their pathogenicity. In dogs, pneumatocysts are considered indicative of chronic infections; however, because pneumatocysts have been observed in cats in as little as 3 wk following infection, that does not appear to apply to cats.[6,11]

As mentioned, two fenbendazole treatment regimens were required to eliminate the *P. kellicotti* infection in the cat described here. Nine days prior to initiation of the second treatment regimen (i.e., day 49), seven focal radiographic lesions were visible in the lungs. All seven nodules were visible 86 days later (day 135). Over the course of treatment, cavitated nodules became solid (2 and 7) and one solid nodule became cavitated (7). Cavitated nodules that became solid may have filled with either fluid or granulation tissue or collapsed on themselves as the parasite(s) died and was resorbed. The solid nodule that became cavitated was the largest nodule. In that case, cavitation likely occurred secondary to central necrosis. Over time, all nodules became smaller and the margins more discrete. The more clearly defined margins were most likely due to less perilesional inflammation during the healing process. One hundred fifty-one days after completion of the second treatment regimen (day 221), one nodule was no longer radiographically evident, and after 246 days (day 316), three of the original seven nodules were no longer evident. Thus, at 246 days following completion of the second fenbendazole treatment regimen, four of the original seven focal radiographic lung lesions were still visible. In earlier work, the rate of resolution of radiographic lung lesions was evaluated in eight naturally infected cats after treatment with albendazole (25 mg/kg PO *q* 12 hr for 11–24 days). Of 21 focal lesions that were visible at initiation of treatment, 7 had completely resolved by day 33, and 13 of 14 lesions had completely resolved after 83–119 days.[9] In cats that were experimentally infected with *P. kellicotti* for 77–101 days, a reduction in the number and size of focal radiographic lung lesions was evident 7–19 days after treatment with albendazole. The duration of time to complete resolution was not described.[8] In cats that were experimentally infected with *P. kellicotti* for 63 days, treatment with praziquantel was associated with a marked reduction/disappearance of radiographic lung lesions at 28 days after treatment; however, the duration of time to complete resolution of lesions was not determined.[11] Collectively, the results indicate that a reduction in the number and appearance of radiographic lung lesions over time may be used in combination with examination of feces for parasite eggs to monitor the success of treatment.[9] Although the duration of complete resolution of radiographic lesions can be highly variable (e.g., up to >246 days in the case described herein), shedding of eggs typically has ceased by 10 days following initiation of successful treatment.

Although pneumothorax was not observed in this case, it should be noted that mild to severe spontaneous pneumothorax may be associated with *P. kellicotti* infections in both cats and dogs, which may reoccur after therapy.[2,5,6] It has also been suggested that clinically inapparent pneumothorax may be a common occurrence in feline infections.[2] Other sequelae that can occur in cats and dogs include pneumonia, peribronchial infiltration that typically is most severe in areas adjacent to *P. kellicotti* lesions, and mild free pleural fluid.[5,6,14]

Conclusion

Two treatment regimens of fenbendazole (28 mg/kg PO *q* 12 hr for 21 days) combined with prednisone were required to eliminate a *P. kellicotti* infection with extensive involvement of the lungs in a cat. In this case, four of seven pulmonary nodules were still radiographically evident at 246 days following completion of successful treatment. Thus, radiographs should not be used as a sole diagnostic test for *P. kellicotti* infections in cats.

FOOTNOTES

[a] SNAP Feline Triple; Idexx Laboratories, Westbrook, ME

[b] QBC Analyzer; QBC Diagnostics Inc., Port Matilda, PA

[c] Safe-Guard Suspension 10%; Intervet Canada Ltd., Whitby, Ontario, Canada

[d] Novo-Prednisone; Novopharm, Toronto, Ontario, Canada

REFERENCES

1. Bowman DD, Hendrix CM, Lindsay DS, et al. *Paragonimus kellicotti* Ward, 1908. In: *Feline clinical parasitology*. 1st ed. Ames (IA): Iowa State University Press; 2002:172–6.
2. Dubey JP, Stromberg PC, Toussant MJ, et al. Induced paragonimiasis in cats: clinical signs and diagnosis. *J Am Vet Med Assoc* 1978;173(6):734–42.
3. Gesinski RM, Thomas RE, Gallicchio V. Survey of *Paragonimus* in Ohio mink. *J Parasitol* 1964;50:151.
4. Yokogawa M. Paragonimus and paragonimiasis. *Adv Parasitol* 1965; 3:99–158.
5. Pechman RD Jr. Pulmonary paragonimiasis in dogs and cats: a review. *J Small Anim Pract* 1980;21(2):87–95.
6. Pechman RD. The radiographic features of pulmonary paragonimiasis in the dog and cat. *J Am Vet Radiol Soc* 1976;17:182–91.
7. Zajac AM, Conboy GA. Fecal examination for the diagnosis of parasitism. In: *Veterinary clinical parasitology*. 7th ed. Ames (IA): Blackwell Publishing; 2006:3–13.
8. Dubey JP, Hoover EA, Stromberg PC, et al. Albendazole therapy for experimentally induced *Paragonimus kellicotti* infection in cats. *Am J Vet Res* 1978;39(6):1027–31.
9. Hoskins JD, Malone JB, Root CR. Albendazole therapy in naturally-occurring feline paragonimiasis. *J Am Anim Hosp Assoc* 1981;17: 265–9.
10. Plumb DC. *Veterinary drug handbook*. 7th ed. Ames (IA): Wiley-Blackwell; 2011:19–21.
11. Bowman DD, Frongillo MK, Johnson RC, et al. Evaluation of praziquantel for treatment of experimentally induced paragonimiasis in dogs and cats. *Am J Vet Res* 1991;52(1):68–71.
12. Dubey JP, Miller TB, Sharma SP. Fenbendazole for treatment of *Paragonimus kellicotti* infection in dogs. *J Am Vet Med Assoc* 1979; 174(8):835–7.
13. Plumb DC. *Veterinary drug handbook*. 7th ed. Ames (IA): Wiley-Blackwell; 2011:414–7.
14. Rendano VT Jr. Paragonimiasis in the cat: a review of five cases. *J Small Anim Pract* 1974;15(10):637–44.
15. Alden CL, Gay S, Adkins A. Pulmonary trematodiasis in a cat: a case report. *Vet Med Small Anim Clin* 1980;75(4):612–7.
16. Bisgard GE, Lewis RE. Paragonimiasis in a dog and a cat. *J Am Vet Med Assoc* 1964;144:501–7.