

Proliferative sparganosis in a dog

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Case Description—A 21-month-old spayed female Border Collie was examined because of progressive right forelimb lameness, signs of pain, and subcutaneous edema. The dog lived in a fenced yard in Tampa, Fla, that contained a small area of marshy terrain.

Clinical Findings—The subcutis and intermuscular fascia contained multiple cystic cavities filled with larval cestodes (plerocercoids or spargana) and cloudy red fluid. Parasites were identified morphologically and by DNA sequence analysis as pseudophyllidean cestodes, most likely *Sparganum proliferum*. The dog developed a progressively worsening fever, dyspnea, mature neutrophilia, and hypoproteinemia. Septic pleuritis and peritonitis complicated the later stages of the disease.

Treatment and Outcome—Treatment with praziquantel, fenbendazole, and nitazoxanide failed to control the proliferation and dissemination of larval cestodes. The dog was euthanized after 133 days of treatment. At necropsy, numerous parasitic tissue cysts were present in the subcutis and intermuscular fascia; these cysts were most abundant in the soft tissues of the forelimbs and cervical musculature. The pleural and peritoneal cavities contained multiple larval cestodes and were characterized by neutrophilic inflammation and secondary bacterial infection.

Clinical Relevance—Findings indicated that clinical signs associated with proliferative sparganosis in dogs may be rapidly progressive and that the condition may be refractory to antiparasitic treatment. Veterinarians should be aware of this zoonotic, water-borne agent. (*J Am Vet Med Assoc* 2008;233:1756–1760)

A 21-month-old 21.4-kg (47.1-lb) spayed female Border Collie was examined because of progressive right forelimb lameness of 2 weeks' duration. Results of a physical examination were unremarkable, and rectal temperature was within reference limits. The dog was treated with carprofen (4.4 mg/kg [2 mg/lb], PO, q 12 h) for 7 days, but the lameness became more severe over the next 4 weeks, to the point that the dog would not bear weight on the limb. Pitting subcutaneous edema developed in the right axillary region and extended to the mid portion of the right forelimb, right axilla, ventral aspect of the neck, and left axilla. The skin overlying the right axilla and forelimb contained several well-defined areas of deep-red discoloration overlying 1- to 3-cm-diameter firm nodules within the subcutis and subjacent soft tissues. Results of a CBC and serum biochemical profile were unremarkable, and radiography of the right forelimb revealed diffuse soft tissue swelling but no skeletal abnormalities. The dog was treated with ciprofloxacin (15 mg/kg [6.8 mg/lb], PO, q 12 h) and carprofen (4.4 mg/kg, PO, q 12 h) for 10 days with no improvement.

Over the following 2 weeks, subcutaneous edema and soft tissue swelling worsened to extend along the entire right forelimb to the level of the carpus, right axilla, ventral aspect of the neck, and left axilla. Signs of pain were evident during palpation of all edematous ar-

eas, and palpation of the nodular areas resulted in signs of intense pain. At this time, results of thoracic radiography and a CBC were normal, but rectal temperature was high (39.3°C [102.7°F]). The dog was treated with dexamethasone sodium phosphate (1.5 mg/kg [0.68 mg/lb], IV, once), amoxicillin-clavulanic acid (18 mg/kg [8.2 mg/lb], PO, q 12 h for 7 days), and tramadol (2 mg/kg [0.9 mg/lb], PO, q 8 to 12 hours as needed for pain).

Two days later, a biopsy specimen was obtained from a nodule adjacent to the triceps brachii muscle, and radiographs of the entire right shoulder region were obtained. Soft tissue swelling had decreased slightly by this time. No skeletal abnormalities were seen on radiographs of the right shoulder region, but linear radiolucent lines could be seen within the soft tissues cranial to the shoulder joint. Histologic examination of the biopsy specimen revealed fibroplasia and chronic panniculitis.

Swelling and signs of pain continued to progress over the next 10 days. Skin overlying the right axilla, ventral aspect of the chest, and right forelimb developed several well-defined areas of deep-red discoloration (ecchymotic hemorrhages), and several 1- to 3-cm-diameter firm nodules could be identified within the subcutis and subjacent soft tissues. Suspecting that the initial biopsy had not yielded diagnostic tissues, the veterinarian conducted a second biopsy. An incision into one of the discolored areas in the right axilla revealed an approximately 2-cm-diameter cystic cavity containing coiled aggregates of many (> 100) intact and fragmented white worms ranging from 10 to 30 mm in length and 2 to 4 mm in width. The cavity was traced and found to extend from the right axilla deep to the

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right pectoral muscle medially and cranially to the left thoracic inlet. The cavity also extended subcutaneously laterally and distally to the point of the right elbow. Flushing the cavity with saline (0.9% NaCl) solution (approx 5 L) produced multiple live worms. A Penrose drain was placed in the pocket and sutured to the skin, and the incision was closed.

Initial anthelmintic treatment included praziquantel (20 mg/kg [9.1 mg/lb], PO, q 24 h for 5 days) and fenbendazole (50 mg/kg [22.7 mg/lb], PO, q 24 h for 3 days). The worms were tentatively identified as tetrahyridia of *Mesocostoides* spp. Therefore, treatment with fenbendazole was continued at a higher dosage (100 mg/kg [45.5 mg/lb], PO, q 12 h for 28 days). Over the next few days, flushing of the cavity with sterile saline solution yielded additional live parasites. Signs of pain and swelling of the right forelimb and axilla subsided for 1 week, but the tissues remained firm and cool. The dog continued to be profoundly lame, and a large fluid-filled bulla formed in the skin overlying the sternum. Before the bulla was ruptured, worms could be seen floating freely in serosanguinous fluid within the bulla. Thoracic radiography was repeated to determine whether there was any thoracic involvement, but results were normal.

Samples of the worms were submitted to the Diagnostic Parasitology Service of the Department of Pathobiology at the Auburn University College of Veterinary Medicine for identification. The worms were identified as larval cestodes, plerocercoids, or spargana of a pseudophyllidean tapeworm, most likely *Spirometra* spp. Seven days after surgery, the Penrose drain was left in place because live worms and copious amounts of serosanguinous fluid were still recovered from the drain openings.

Treatment with fenbendazole was continued at the same dosage (100 mg/kg, PO, q 12 h), and cefpodoxime proxetil (2.5 mg/kg [1.1 mg/lb], PO, q 24 h for 10 days) and metronidazole (24 mg/kg [10.9 mg/lb], PO, q 12 h for 7 days) were added to the treatment regimen. The dog was referred to the University of Florida Veterinary Teaching Hospital for further diagnostic testing and treatment.

At the Veterinary Teaching Hospital, thoracic and abdominal ultrasonography revealed mild pleural and peritoneal effusions. Treatment with fenbendazole (100 mg/kg, PO, q 12 h) was continued, and praziquantel (50 mg/kg, SC, divided among 6 sites) was given once a week for 3 weeks. Moderate soft tissue swelling and signs of pain were noticed at injection sites for several days after praziquantel was administered. The Penrose drain was removed 2 weeks after surgery, but moderate amounts of serosanguinous fluid continued to drain from the wound.

Swelling of the right forelimb and signs of pain subsided somewhat, and for 3 weeks, no plerocercoids (spargana) were observed in fluid draining from the wound. However, several new bullae developed over the ventral aspect of the thorax, right side of the neck, and right axillary region, and serous fluid developed in the thorax. Treatment with fenbendazole (100 mg/kg, PO, q 12 h) and praziquantel (50 mg/kg, SC, once a week) was continued.

After 28 days, treatment with fenbendazole was discontinued. At this time, all wounds were healing and signs of pain were less severe, although the dog continued to have signs of moderate to severe pain and swelling at praziquantel injection sites. One week after the third praziquantel injection, the dog developed dyspnea and fever (40.3°C [104.5°F]), and new lesions erupted on the ventral aspect of the chest and in the right axilla. The dog had a poor appetite and had lost 1.5 kg (3.3 lb) over the past 2 weeks. Radiography revealed an effusion within the right pleural cavity, and thoracocentesis yielded approximately 500 mL of cloudy serosanguinous fluid. A CBC and serum biochemical profile revealed mild anemia, mild monocytosis, and moderate hypoalbuminemia, but WBC count was within reference limits. Treatment with enrofloxacin (3.5 mg/kg [1.6 mg/lb], PO, q 12 h) was begun, and a sample of the pleural fluid was submitted for bacterial culture. *Pseudomonas aeruginosa* susceptible to enrofloxacin was obtained.

The dog was treated with praziquantel (30 mg/kg [13.6 mg/lb], PO, q 24 h) for 8 days. Within 2 weeks, the dog developed a pendulous abdomen, and abdominocentesis yielded 2.3 L of serosanguinous fluid. Cytologic examination of the fluid revealed scattered segmented neutrophils, but no bacteria were seen. The dog's appetite continued to be poor, and the dog had lost an additional 1.5 kg during this 2-week period. Nitazoxanide (500 mg, PO, q 12 h) was administered for 2 weeks, in addition to enrofloxacin and carprofen, but the dog's anorexia became worse, and the dog began vomiting. Metoclopramide (0.3 mg/kg [0.14 mg/lb], SC, then 0.3 mg/kg, PO, q 12 h as needed for vomiting) and famotidine (0.5 mg/kg [0.23 mg/lb], IM, then 0.5 mg/kg, PO, q 12 h) were administered.

The dog's overall body condition and attitude deteriorated dramatically, although body weight was still 18.5 kg (40.7 lb) because of fluid accumulations in the thoracic and abdominal cavities. The owners elected to euthanize the dog, and the body was submitted to the Anatomic Pathology Service of the Department of Pathobiology at the Auburn University College of Veterinary Medicine for necropsy.

At necropsy, the subcutis and intermuscular fascia of the right forelimb, right axilla, ventral thoracic midline, and ventral cervical region contained many inflammatory tissue cysts filled with nodules of entangled intact and degenerate white larval cestodes (spargana) surrounded by red, cloudy, thick fluid (Figure 1).



Figure 1—Postmortem photograph of an inflammatory tissue cyst within the intermuscular fascia of the right axilla in a dog with proliferative sparganosis. Notice the many entangled spargana within the cyst. Bar = 15 mm.

There was severe atelectasis of the right lung, and the right pleural cavity contained about 150 mL of thick, cloudy, tan fluid with 2 larval cestodes and scattered white, friable fragments. There was partial atelectasis of the left lung, and the left pleural cavity contained about 100 mL of cloudy tan fluid with several free-floating larval cestodes. Microscopic examination of smears of the pleural fluid stained with Wright-Giemsa stain revealed many bacteria both extracellularly and within neutrophils. The peritoneal cavity contained about 250 mL of red, cloudy fluid, and microscopic examination of the fluid revealed many bacteria and segmented neutrophils. There were many fibrous adhesions between the omentum and serosal surfaces of the small intestine, spleen, and stomach. At least 2 larval cestodes were present in the peritoneal fluid. Cestodes were frozen immediately for DNA analysis and fixed in glutaraldehyde and 10% formalin.

Histologically, parasitic cysts were characterized by chronic pyogranulomatous myositis associated with draining tracts that contained plerocercoid larvae (Figure 2). The pleura and lungs were characterized by pyogranulomatous pleuritis and severe pulmonary atelectasis. There was severe pyogranulomatous peritonitis in conjunction with fibrosis of the serosa and omentum. The pleural and peritoneal cavities contained scattered plerocercoid larvae and abundant bacteria. The larvae lacked a digestive tract and demonstrated frequent but shallow invaginations of the tegument but no strobilation. Parenchymal cavities were lined by tegument and were often filled with a granular intensely eosinophilic substance. Microtriches projected from the surface of the tegument. In some areas, subtegumentary cells formed palisades beneath the densely eosinophilic tegumentary syncytium. The body was comprised of evenly distributed, loose parenchyma with calcareous corpuscles, muscle fibers, and excretory ducts (Figure 3). No genitalia were present. Muscle fibers were loosely arranged in a discontinuous row that was oriented parallel to the tegument. In some areas, muscle fibers were arranged haphazardly through the body. Scolices were not present; however, deep invaginations suggestive of holdfast bothria could be identified. Larvae were surrounded by hemorrhage, mixed inflammation (macrophages, lymphocytes, and neutrophils), and deeply eosinophilic aggregates of granular substance and calcareous corpuscles occasionally forming spheric concretions within the tissues. Some sections of larval cestodes had an amphiphilic tegument with no discernible invaginations (dead larvae). The walls of cavities containing dead larvae had extensive fibrosis and fibroplasia. Other sections had a brightly eosinophilic tegument with prominent invaginations (viable larvae). There was regional myofiber loss, with replacement by fibrosis. The right axillary lymph node was severely atrophied and edematous, and subcapsular sinuses contained multiple aggregates of eosinophilic amorphous substance similar to that surrounding the larvae in tissue cysts.

Nucleic acid was extracted from intact frozen spargana with a robotic extractor⁹ used in accordance with the manufacturer's directions, and a PCR assay incorporating eucestode primers 84 and 90 was used to amplify a fragment of the 18S rDNA, as described.¹ Amplicons were sequenced at the Oklahoma State University core



Figure 2—Photomicrograph of a section of a tissue cyst from the dog in Figure 1. Notice the multiple cross sections of spargana (arrows), the abundant space around individual spargana, and the capsule (C) consisting of amorphous eosinophilic material and relatively few inflammatory cells. H&E stain; bar = 500 μ m.

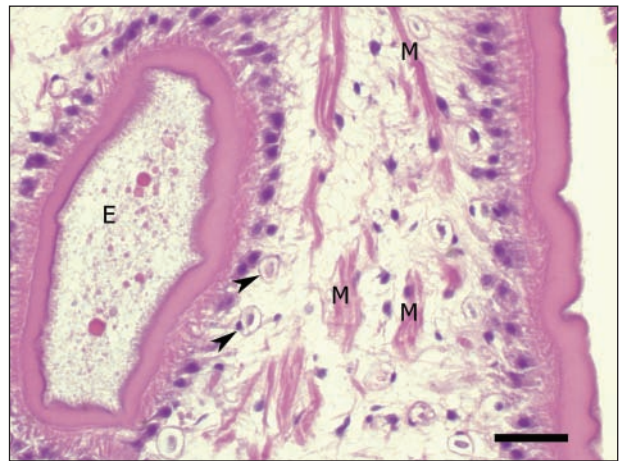


Figure 3—Photomicrograph of a sparganum from the dog in Figure 1. The tegument is characterized by invaginations resulting in segmentation, and columnar subtegumentary cells form a row beneath the densely eosinophilic tegumentary syncytium. The body is comprised of evenly distributed loose parenchyma with calcareous corpuscles (arrowheads), muscle fibers (M), and excretory ducts (E). Muscle fibers are loosely arranged in a discontinuous row parallel to the tegument. H&E stain; bar = 20 μ m.

facility with a capillary sequencer, and sequences were compared with reported sequences for *Spirometra erinacei* (D64072), *Diphyllobothrium latum* (AM778553), *Mesocostoides corti* (AF286984), and *Taenia solium* (DQ157224). Amplicon sequences (EU392209) most closely resembled (99.4% identical) previously reported sequences for pseudophyllidean cestodes.

Discussion

Clinical signs in the dog described in the present report were attributed to proliferative sparganosis caused by proliferating larval cestodes (spargana) of *Sparganum proliferum*.^{2,3} Spargana were widely distributed throughout the soft tissues, including the intermuscular fascia of the cranial half of the body, and within the pleural and peritoneal cavities. The body cavity parasitism was

associated with chronic pleuritis and peritonitis caused by infection with *P aeruginosa*. The proximity of the axillary and cervical parasitic cysts to the thoracic inlet suggested that bacterial pleuritis resulted from septic inflammation associated with larval migration into the pleural cavity. Presumably, the bacteria entered the body through draining cutaneous tracts that communicated with parasitic cysts. As the parasitism extended caudally along the sternum, a similar process may have resulted in septic peritonitis.

Sparganosis is a disease characterized by the presence of spargana in host tissues.⁴ There are 2 forms of sparganosis: nonproliferative and proliferative.⁵ Most infections are nonproliferative and are associated with the presence of a single larva of *Spirometra erinaceieuropaei* or *Spirometra mansonioides*. Proliferative sparganosis is caused by asexual replication of larvae of *S proliferum* in host tissues and the migration of these larvae to new tissues, where they grow and repeat the process, ultimately resulting in the death of the host.⁶ In 2001, *S proliferum* was identified phylogenetically as a new species in the order Pseudophyllidea.² Previously, it was thought that *S proliferum* was a separate species closely related to *S erinaceieuropaei*⁷ or that *S proliferum* was an abnormally differentiated form of *S erinaceieuropaei*.^{8,9}

Human infection with a proliferating plerocercoid larval cestode was first described in 1905,⁷ and the first human infection in the United States was reported in 1908.¹⁰ Other cases have been reported in South America and Asia.^{3,5,11-14} Infection with *S proliferum* in cats, dogs, and feral hogs has also been reported,^{6,15-17} but to the authors' knowledge, proliferative sparganosis involving a dog in North America has not been reported previously.

Without genetic confirmation, it would be difficult to definitively distinguish between infections caused by *S proliferum* and infections caused by *Spirometra* spp. In the case of *Spirometra* infection, the pattern of disease induced by consumption of many plerocercoids or procercoids would be one of multifocal lesions containing solitary or small numbers of larvae distributed somewhat evenly throughout the body. In contrast, in the dog described in the present report, the infection was initially characterized by development of encysted plerocercoid larvae in the right axilla, suggesting that the disease resulted from a single initial nidus of infection and emanated from that point as larvae proliferated within cystic cavities.

The life cycle of *S proliferum* has not yet been confirmed,³ but probably resembles life cycles of related pseudophyllidean tapeworms of the genus *Spirometra*,¹⁸⁻²⁰ with the exception that *S proliferum* includes a stage of asexual multiplication within intermediate or paratenic hosts. Adult tapeworms reside in the intestinal tract of definitive hosts, including dogs and other carnivores, and operculated ova are discharged from the uterine pore of adult tapeworms and shed in the feces. The operculated ova hatch in water, releasing a ciliated intermediate form (coracidium). Coracidia are ingested by the first intermediate host, a copepod crustacean (*Cyclops* spp), and develop into the procercoid stage. After infected copepods are ingested by the second intermediate host (any vertebrate other than a fish), the

procercoids develop into plerocercoids (spargana) and migrate throughout the soft tissues of the body. If the second intermediate host is eaten by another nonfish vertebrate serving as a transport host, the plerocercoids migrate through the tissues but remain as plerocercoids. Larval forms of *Spirometra* spp can infect and survive in a series of transport hosts until finally consumed by a carnivore definitive host.²¹ Once ingested by the definitive host, the plerocercoids develop into adults, with ova evident in the host's feces 10 to 30 days after infection.^{15,17,18,21} Dogs can become infected in 3 different ways: through ingestion of water contaminated with copepods carrying procercoids, direct infection of open wounds with plerocercoids, or ingestion of plerocercoids in transport vertebrate hosts.^{3,18} Owing to the fact that the first intermediate host is aquatic, sparganosis is usually associated with exposure to aquatic environments that contain infectious forms of the cestode. In the present case, the dog was presumably exposed to *S proliferum* in a marshy region of the yard where it lived, which communicated with a wetland conservation area. After a definitive diagnosis was made, the owner was advised to limit the dog's exposure to the aquatic environment in an effort to prevent subsequent infection. A dog living in an adjacent lot and exposed to the same marshy environment remained clinically normal throughout the time the dog described in the present report was treated. Neither a survey of infection in possible transport and intermediate hosts nor an analysis of water samples in the dog's environment was conducted.

Sparganosis is zoonotic; thus, precautions should be undertaken to prevent human infection through consumption of infected water or insufficiently cooked fish or game or the application of infected medicinal poultices to wounds. It is interesting to note that the first human case of proliferative sparganosis in North America was reported¹⁰ in 1908 in a Florida resident living in the same geographic region as the dog described in the present report.

Currently, there are no products labeled for treatment of *Spirometra* infection in dogs.²¹ Use of albendazole (25 mg/kg [11.4 mg/lb], PO, q 12 h for 10 days) has proven to be ineffective, as has administration of niclosamide (333 mg/kg [151 mg/lb], PO, once).²² The standard dose of praziquantel (5 mg/kg [2.3 mg/lb], PO, once) is not effective,²² but administration at a higher dosage (7.5 mg/kg [3.4 mg/lb], PO, q 24 h for 2 days) has been effective,²³ although it was not effective in the dog described in the present report. In humans with proliferative sparganosis, treatment with mebendazole and praziquantel has also proven ineffective and has been associated with various adverse effects, including severe nausea, vomiting, gastritis, sinus tachycardia, muscle tenderness, and a burning sensation at the injection site.²⁴ In the dog described in the present report, nitazoxanide was administered during the later stages of treatment. Nitazoxanide is an antiprotozoal drug approved for use in humans that has been shown in preclinical trials to be efficacious against cestodes. However, efficacy of nitazoxanide against *S proliferum* could not be evaluated in the present case because of how advanced the disease was at the time the drug was

first administered. As illustrated in the present case, the lack of treatment options for proliferative sparganosis warrants a poor prognosis for survival. Infection of dogs is best controlled by preventing the consumption of contaminated water or the ingestion of vertebrates that could serve as second intermediate hosts.

a. Maxwell 16, Promega Corp, Madison, Wis.

References

- Mariaux J. A molecular phylogeny of the Eucestoda. *J Parasitol* 1998;84:114–124.
- Miyadera H, Kokaze A, Kuramochi T, et al. Phylogenetic identification of *Sparganum proliferum* as a pseudophyllidean cestode by the sequence analyses on mitochondrial COI and nuclear *sdhB* genes. *Parasitol Int* 2001;50:93–104.
- Nakamura T, Hara M, Matsuoka M, et al. Human proliferative sparganosis. A new Japanese case. *Am J Clin Pathol* 1990;94:224–228.
- Noya O, Alarcon de Noya B, Arrechdera H, et al. *Sparganum proliferum*: an overview of its structure and ultrastructure. *Int J Parasitol* 1992;22:631–640.
- Moulinier R, Martinez E, Torres J, et al. Human proliferative sparganosis in Venezuela: report of a case. *Am J Trop Med Hyg* 1982;31:358–363.
- Buergelt CD, Greiner EC, Senior DF. Proliferative sparganosis in a cat. *J Parasitol* 1984;70:121–125.
- Ijima I. On a new cestode larva parasitic in man. *J Coll Sci Imp Univ Tokyo* 1905;20:1–21.
- Iwata S. Some experimental studies on the regeneration of the plerocercoid of Manson's tapeworm, *Diphyllobothrium erinacei* (Rudolphi) with special reference to its relationship with *Sparganum proliferum*. *Jpn J Zool* 1934;6:139–158.
- Mueller JF. *Sparganum proliferum*, a sparganum infected with a virus? *J Parasitol* 1974;60:15–19.
- Stiles W. The occurrence of a proliferating cestode larva (*Sparganum proliferum*) in a man in Florida. *Bull Hygienic Lab* 1908;40:7–18.
- Beaver PC, Rolon FA. Proliferating larval cestode in a man in Paraguay. A case report and review. *Am J Trop Med Hyg* 1981;30:625–637.
- Lin T, Su I, Lu S, et al. Pulmonary proliferating sparganosis. A case report. *J Formos Med Assoc* 1978;77:467–472.
- Morishita K. Rare human tapeworms reported from Japan V. *Sparganum proliferum* (Ijima 1905). *Prog Med Parasitol Jpn* 1972;4:478–488.
- Yoshida S. On a second and third case of infection with *Plerocercoides prolifer* Ijima, found in Japan. *Parasitology* 1914;7:219–225.
- Bengtson SD, Rogers F. Prevalence of sparganosis by county of origin in Florida feral swine. *Vet Parasitol* 2001;97:239–242.
- Beveridge I, Friend SC, Jeganathan N, et al. Proliferative sparganosis in Australian dogs. *Aust Vet J* 1998;76:757–759.
- Gray ML, Rogers F, Little S, et al. Sparganosis in feral hogs (*Sus scrofa*) from Florida. *J Am Vet Med Assoc* 1999;215:204–208.
- Mueller JF. The biology of *Spirometra*. *J Parasitol* 1974;60:3–14.
- Olsen DW. *Animal parasites: their biology and life cycles*. Minneapolis: Burgess Publishing Co, 1962.
- Wirth WA, Farrow CC. Human sparganosis: case report and review of the subject. *JAMA* 1961;177:6–9.
- Little S, Ambrose D. *Spirometra* infection in cats and dogs. *Compend Contin Educ Pract Vet* 2000;22:299–306.
- Kirkpatrick CE, Sharninghausen F. *Spirometra* sp infection in a cat in Pennsylvania. *J Am Vet Med Assoc* 1983;183:111–112.
- Hendrix C. Helminthic infections of the feline small and large intestines: diagnosis and treatment. *Vet Med* 1995;90:456–472.
- Torres JR, Noya OO, Noya BA, et al. Treatment of proliferative sparganosis with mebendazole and praziquantel. *Trans R Soc Trop Med Hyg* 1981;75:846–847.