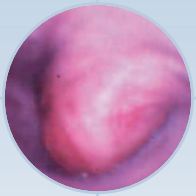

Canine Spirocercosis

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ABSTRACT: Spirocercosis (*Spirocerca lupi*) in dogs has been mostly associated with the presence of esophageal granulomas that may transform to sarcomas; aortic aneurysms; mid-thoracic spondylitis; hypertrophic osteopathy; salivary gland necrosis; and pyothorax. Although the disease is frequently subclinical, esophageal dysphagia manifested by regurgitation, odynophagia, and hypersalivation is considered the clinical hallmark. Diagnosis should combine fecal analysis, thoracic radiography, and esophagoscopy to look for parasite ova, spondylitis or posterior mediastinal masses, and parasite nodules or tumors, respectively. Two avermectins, doramectin and ivermectin, have been effective in the treatment of canine spirocercosis, resulting in clinical remission, regression, or elimination of esophageal granulomas and cessation of egg shedding.

Spirocercosis, caused by the spirurid nematode *Spirocerca lupi* (Rudolphi 1809), has a worldwide distribution, mostly occurring in warm climates, and a prevalence that varies considerably, even between close geographic areas.[1–3] In the United States, the area with the highest prevalence of the disease extends from Alabama through Mississippi to Oklahoma and at least a part of Texas.[1] Although spirocercosis affects carnivorous animals other than dogs,[1] the major epidemiologic drivers of the disease include canine population density and environmental conditions (e.g., soil type and pH, temperature, rainfall, solar radiation) that sustain the source of the intermediate hosts.[4] An urban pattern of distribution has been documented in Israel,[5] while a rural pattern exists in Kenya and South Africa[3,6,7]; in Greece, spirocercosis is equally common in urban and rural areas.[8]

LIFE CYCLE

Adult *S. lupi* are pink-red, lengthy (males and females measure approximately 1½ to 2 inches [3 to 4 cm] and 3 to 3½ inches [6 to 7 cm], respectively) worms that reside within intramural granulomatous nodules located in the distal thoracic esophagus.[1,9] Following a prepatent period of 4 to 6 months,[10] the deposited embryonated eggs pass into the esophageal lumen through small fistulous tracts. Depending on the female worm population, infected dogs may continuously or intermittently shed large numbers of eggs, frequently in excess of one million per day.[1] Dogs are infected by ingesting third-stage larvae–laden dung beetles (intermediate hosts) or by feeding on transport hosts (e.g., reptiles, birds, rodents) that have preyed on beetles.[11,12] The infective larvae are released into the stomach, penetrate its mucosa, and begin a strikingly predictable migration, reaching the thoracic aorta within 3 weeks.[9] Most of the larvae leave the aorta approximately 3 months after

infection and cross over to the esophagus, where they incite the development of granulomatous nodules as they mature to adults over the next 3 months.[1,9] Aberrant migrations to unusual locations, particularly in the thoracic cavity, may also occur.[9,13] The postinoculation life span of adult worms has been estimated at 738 days.[1]

PATHOGENESIS

Esophageal granulomas and sarcomas (fibrosarcomas, osteosarcomas, undifferentiated sarcomas), aortic aneurysms and thrombosis, thoracic diskospondylitis and spondylosis, hypertrophic osteopathy, salivary gland necrosis, and pyothorax have all been associated with larval migration and the localization of adult worms within host tissues.[3,8,9,14–17] The pathogenesis of *S. lupi*–associated sarcomas has yet to be elucidated.[18] Proposed mechanisms include the malignant transformation of fibroblasts within the granulomatous reaction, the inciting role of an oncogenic stimulus originating from the parasite itself, and even environmental factors.[1,9,15,18] Sarcomas are almost exclusively localized to the esophagus,[9] with a single sarcoma reported at an aberrant migratory site.[14] Prevalence of infection does not influence the rate of sarcoma development; sarcomas have not been noticed in some geographic areas where *S. lupi* is highly endemic.[9] Further studies should be undertaken to elucidate the epidemiology and the prevalence of sarcoma formation in canine spirocercosis. The recently established murine xenograft model of *S. lupi*–associated sarcomas may facilitate studies addressing the factors related to parasite-triggered tumorigenesis.[18]

Granulomas and sarcomas may result in esophageal dysphagia due to mechanical obstruction and, possibly, functional impairment.[8,19] Esophageal dysphagia may be worsened by concomitant salivary gland necrosis associated with *S. lupi* infection.[16] Respiratory distress and coughing have been attributed to the space-occupying nature of voluminous granulomatous or neoplastic masses, pulmonary metastases of the latter, dysphagia-induced aspiration bronchopneumonia, and, occasionally, esophageal wall perforation leading to mediastinitis or pyothorax.[2,14,20,21] Ulceration of granulomas or sarcomas may lead to melena without hematemesis[8,19] and chronic hemorrhagic anemia.[3,14,19,22] Aortic scars, aneurysms, and, more rarely, ossification or local thrombosis may result from the larvae burrowing through the aortic wall[3,17,23,24]; fatal hemothorax may occur secondary to sudden aortic rupture.[23,25–27] Spondylitis or spondylosis that can lead to lameness or even paraplegia has been attributed to periosteal irritation or to the obstruction of intervertebral arteries by migrating juvenile worms.[13] Gait abnormalities have also been ascribed to hypertrophic osteopathy, an uncommon sequel of sarcomas that may be the result of vagal stimulation followed by hypervascularity, arteriovenous anastomosis, and periosteal reaction.[9] Aberrant migration of *S. lupi* larvae may cause a wide spectrum of atypical clinical manifestations, including hemopericardium, congestive heart failure due to aorticopulmonary shunting, anterior vena cava syndrome, vomiting, and subcutaneous nodules.[8,13,28,29] Concurrent infectious and parasitic diseases such as leishmaniasis (*Leishmania infantum*), monocytic ehrlichiosis (*Ehrlichia canis*), and dirofilariasis (*Dirofilaria immitis*) have been documented in 36% of dogs with spirocercosis and may account for the complicated clinical picture of the disease.[8]

Esophageal dysphagia is the clinical hallmark of spirocercosis in dogs.

CLINICAL AND CLINICOPATHOLOGIC FINDINGS

S. lupi infection is usually subclinical.[3,30] Young adult and large-breed dogs are apparently more prone to develop clinical spirocercosis, with Labrador retrievers, German shepherds, and Hellenic hounds being overrepresented.[5,8,22,31] When the infection is clinically evident, it is mainly manifested by regurgitation, repeated attempts to swallow (odynophagia), and hypersalivation.[5,8,22] Vomiting, melena, decreased appetite, progressive loss of body weight, weakness, dyspnea, coughing, fever, lameness, paraparesis, swollen distal limbs, and salivary gland enlargement are less common clinical signs of this parasitic disease.[5,8,22,31] However, melena or dyspnea may be the sole presenting complaint.[5,8]

Normocytic, normochromic, nonregenerative anemia, neutrophilic leukocytosis, hyperproteinemia, and increased alkaline phosphatase and creatine kinase activities have been recently proposed as useful, although

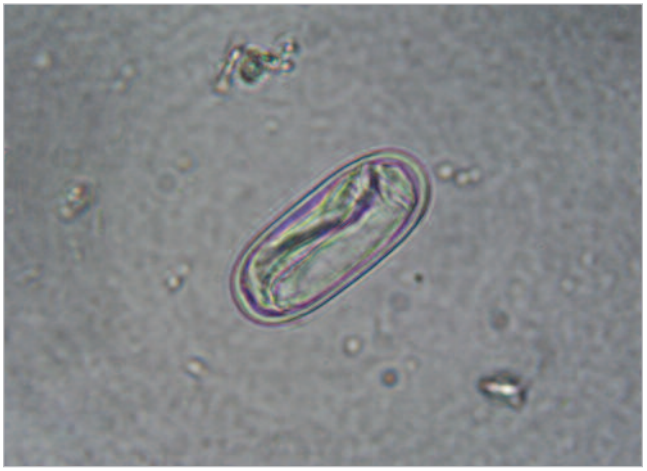


Figure 1. *Spirocerca lupi* embryonated egg (Teleman's method, 1000×).

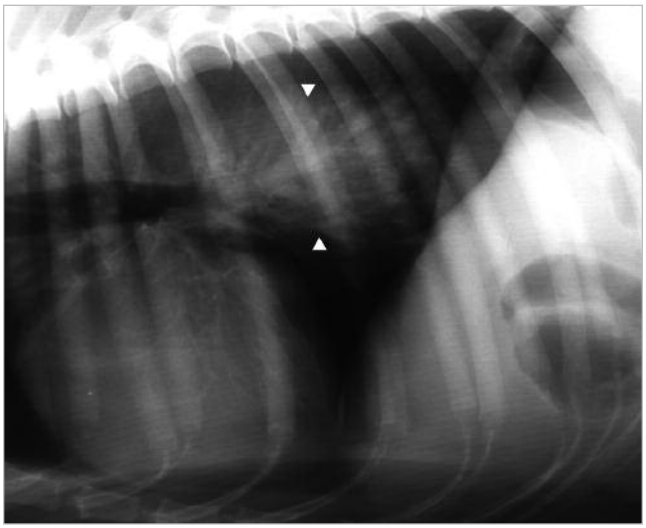
nonspecific, clinicopathologic indicators of clinical spirocercosis.[5,8]

DIAGNOSTIC CONSIDERATIONS

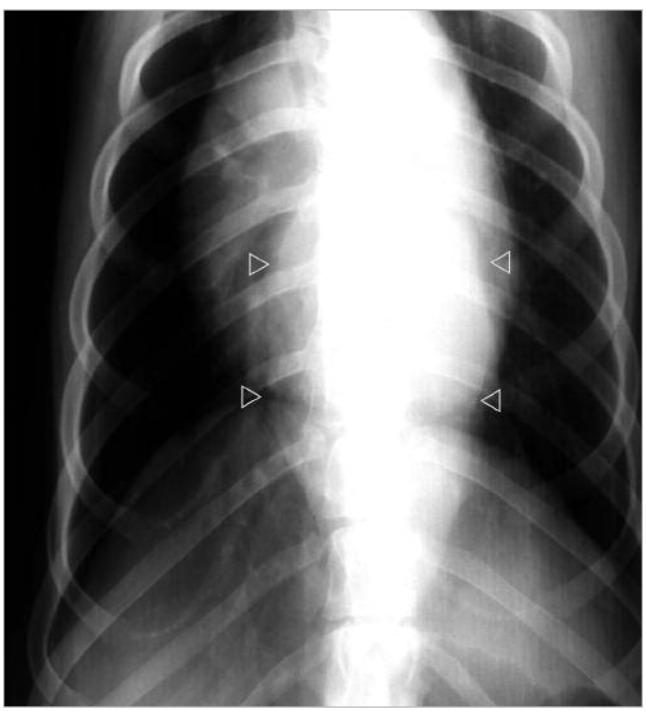
Spirocercosis, either clinical or subclinical, is diagnosed by means of fecal analysis. Sugar flotation (specific gravity 1.270), Teleman's sedimentation, and fecal dilution with artificial gastric juice are the techniques usually applied to find the embryonated, thick-shelled, small (30 to 37 µm by 11 to 15 µm) parasitic ova[30,32,33] (Figure 1). Methods such as flotation with zinc sulfate (specific gravity 1.142) or sodium nitrate (specific gravity 1.200) solutions are reportedly of inferior diagnostic yield.[22,34–36] Regardless of the method used, false-negative results have been ascribed to unisex or prepatent infections, intermittent egg shedding, aberrant parasite migrations, and neoplastic transformation of the parasitic granulomas.[9,19] Therefore, negative fecal examination results do not definitely rule out spirocercosis, and serial examinations of fecal samples collected on consecutive days may be warranted to increase the diagnostic sensitivity.[5,8] Ova may still be detected up to 2 weeks after the institution of adulticide treatment.[37]

Survey thoracic radiography is less sensitive and specific than fecal analysis or esophagoscopy, but it frequently allows the detection of parasite-induced lesions or their secondary complications. The prominent radiographic features associated with *S. lupi*–induced lesions are caudal thoracic spondylitis and a caudodorsal mediastinal mass (Figure 2) that may represent a *S. lupi*–induced granuloma, sarcoma, hematoma, or abscess.[5,8,22] The presence of both features is strongly suggestive of spirocercosis in areas where the disease is endemic. Intraluminal air accumulation, anterior mediastinal masses, ventral displacement of

Figure 2. Radiographic views of the thorax demonstrating a radiopaque caudodorsal mediastinal mass (*arrowheads*) that may represent a voluminous *S. lupi* granuloma. (From Mylonakis ME, Rallis T, Koutinas AF, et al. Clinical signs and clinicopathologic abnormalities in dogs with clinical spirocercosis: 39 cases [1996-2004]. *JAVMA* 2006;228:1063-1067; with permission)



Lateral view.



Dorsoventral view.

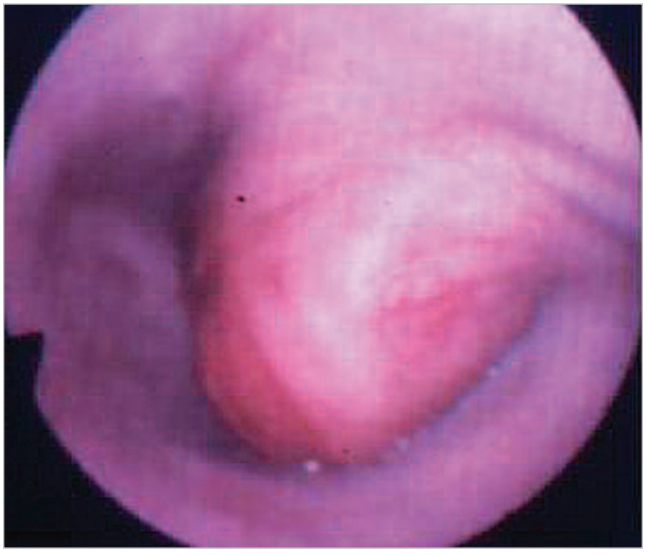


Figure 3. Endoscopic view of an *S. lupi* granuloma protruding into the lumen of the distal thoracic esophagus.

the trachea or mainstem bronchi, an alveolar pattern in the cranial lung lobes, pleural effusion due to hemothorax or pyothorax, pulmonary metastatic disease, pneumothorax, mineralization of the aorta, and cranial mediastinal masses are less common radiographic findings.[5,8,19,22] A barium swallow may outline the esophageal masses or demonstrate a pulsion diverticulum.[7] Although rarely performed in the clinical setting, computed tomography should be considered in cases of extraesophageal disease (i.e., detection of aortic mineralization); as a presurgical screening tool to objectively estimate the size, shape, and intraluminal extension of esophageal nodules; and, perhaps, in the investigation of pulmonary metastases.[22]

Esophagoscopy and, sometimes, gastroscopy are the diagnostic modalities of choice for direct visualization of *S. lupi* nodules. These nodules typically appear as broad-based protuberances with a nipple-like orifice (Figure 3) from which a worm may occasionally protrude.[a] They may be solitary, multiple, smooth, or ulcerated, and they vary in size from an inconspicuous protrusion to a voluminous mass that obstructs most of the esophageal lumen.[5,8] The distal part of the thoracic esophagus (less than 5 inches [10 cm] from the cardia) is the best place to visualize the parasitic nodules.[5] Although esophageal neoplastic masses tend to be pedunculated or cauliflower-like, whereas granulomas typically have a smooth outline, endoscopy does not always help to differentiate *S. lupi*–associated sarcomas from granulomas or from other primary esophageal tumors (e.g., leiomyomas).[19] Notably, endoscopic pinch biopsies may also be misleading because they usually detect superficial inflammation rather than a deep-seated neoplastic process.[19,22] Consequently, surgically obtained esophageal biopsies are essential for reliable histopathologic evaluation of the tissue response (inflammatory or neoplastic) to the parasite.[22]

[a]To see an endoscopic video of *S. lupi*–induced distal esophageal nodules, visit *Compendium*'s Web Exclusives at vetlearn.com.

TREATMENT

Doramectin and ivermectin have recently emerged as the most promising agents in the treatment of naturally acquired and experimental spirocercosis, although their use for this disease is currently off-label. In seven cases of natural infection, administration of doramectin (200 µg/kg SC) at 14-day intervals for three treatments was effective in achieving clinical remission in all cases and eliminating esophageal nodules in five; increasing the dose to 500 µg/kg PO daily for an additional 6-week period led to the complete disappearance of parasitic nodules in the remaining two dogs.[36] Also, in seven experimentally infected dogs with subclinical spirocercosis, doramectin (400 µg/kg SC) administered every 14 days for a total of six treatments, followed by 20 additional monthly injections when the involution of esophageal nodules was incomplete, terminated egg shedding in all cases and eliminated lesions in six dogs.[38] Ivermectin (600 µg/kg SC), administered twice at 14-day intervals, combined with oral prednisolone (0.5 mg/kg) given q12h for 2 weeks and then once daily for an additional week, led to negative results of fecal testing and complete nodular regression in all eight treated dogs; complete clinical remission was accomplished in 87.5% of the dogs, implying the presence of residual esophageal dysfunction.[39] No drug-associated untoward effects were noticed in these studies, but collies and other herding breeds had been excluded. It is prudent to avoid using doramectin or ivermectin in herding breeds at the dose ranges suggested in these studies.[40]

The incidence of esophageal sarcoma may be increased in Spirocerca lupi*–endemic areas.*

Ethanol-induced chemical ablation of *S. lupi* esophageal

nodules was evaluated in six dogs, four of which showed satisfactory clinical remission; however, nodular regression and cessation of egg shedding were rarely achieved.[39] The high cost and inherent risks (i.e., chemical esophagitis and esophageal wall perforation) associated with the use of this method would limit its application to only the avermectin-sensitive herding breeds.[39]

Surgical removal of esophageal nodules or tumors has been largely unsuccessful due to the frequently extensive nature of the lesions and the postsurgical complications.[9,41,42] Recently, the excision of esophageal tumors using a partial esophagectomy technique, with or without complementary doxorubicin-based chemotherapy, appeared to substantially prolong survival time and improve quality of life in dogs with *S. lupi*-associated sarcomas.[19]

PREVENTION

In endemic areas, regularly and properly disposing of fecal material, controlling stray dog populations, avoiding feeding dogs offal from transport hosts, and appropriately treating infected animals may eventually reduce the incidence of spirocercosis.

In contrast to the indisputable effectiveness of doramectin and ivermectin against adult *S. lupi*, the role of these drugs in eliminating the juvenile stages of the parasite still remains elusive. In a recent experimental study, doramectin (400 µg/kg SC at 30-day intervals for three treatments) failed to prevent infection, although the treated dogs developed fewer and smaller esophageal nodules, demonstrated a reduced egg output, and had a higher survival rate than their untreated counterparts.[26] Therefore, the prophylactic use of doramectin necessitates regular follow-up examinations so that new patent infections can be treated appropriately.

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ARTICLE #3 CE TEST

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1. The migratory route of *S. lupi* larvae in the dog most frequently involves the
a. esophagus.
b. lungs.
c. aorta.
d. posterior vena cava.

2. _____ has/have not been seen as the result of canine spirocercosis.
a. Esophageal sarcomas
b. Gastric sarcomas
c. Aortic aneurysms
d. Pyothorax

3. Which type of esophageal sarcoma has not been associated with canine spirocercosis?
a. osteosarcoma
b. fibrosarcoma
c. leiomyosarcoma
d. undifferentiated sarcoma

4. The typical clinical manifestation of canine spirocercosis is
a. vomiting.
b. regurgitation.
c. inspiratory dyspnea.
d. lameness.

5. Sudden death in dogs with spirocercosis most commonly occurs secondary to
a. anemia due to continued bleeding of an ulcerated parasitic granuloma.
b. respiratory compromise due to the presence of voluminous parasitic granulomas.
c. aortic rupture with resultant hemothorax or hemopericardium.
d. pyothorax secondary to mid-thoracic spondylitis.

6. Which biochemical finding is considered a useful indicator in the diagnosis of canine spirocercosis?
a. hyperproteinemia
b. hypoalbuminemia
c. hypoglycemia
d. increased alanine aminotransferase activity

7. The earliest time postinfection that *Spirocerca* ova can be detected by fecal analysis is _____ months.
a. 3
b. 4
c. 6
d. 8

8. Which radiographic feature is strongly suggestive of canine spirocercosis?
a. air accumulation within the esophageal lumen
b. anterior mediastinal mass
c. caudodorsal mediastinal mass
d. mid-thoracic spondylosis deformans

9. Which statement regarding the endoscopic diagnosis of spirocercosis is correct?
a. Endoscopy always differentiates *S. lupi*-induced granulomatous nodules from neoplasia.
b. *S. lupi*-induced granulomas may be located at any distance from the cardia.
c. Endoscopy-guided pinch biopsy is the preferred method of differentiating between granulomatous and neoplastic nodules.
d. Either granulomatous or neoplastic *S. lupi*-associated nodules may resemble other primary esophageal neoplasms.

10. The medical treatment of choice in canine spirocercosis is
a. doramectin or ivermectin.
b. diethylcarbamazine.
c. milbemycin.
d. prednisolone.