Chronic Cough in a Dalmatian

Gary A. Conboy, DVM, PhD, DACVM
Atlantic Veterinary College

A 3-year-old intact male Dalmatian presented for a persistent and progressively worsening cough of approximately 1-month duration.

History

Vaccinations were up-to-date. The dog and the client had spent about 1 year in Copenhagen, Denmark, and the dog developed the nonproductive cough approximately 2 months after returning to the United States. A heartworm antigen test performed shortly thereafter was negative.

Physical Examination

The dog appeared lethargic and depressed. His weight was 28 kg, and body condition was normal. Hydration was normal. The dog's temperature and pulse were also normal, but respiratory rate was elevated at 64 breaths/minute. No abnormal heart or lung sounds were detected on auscultation. A cough was elicited on tracheal palpation. The dog coughed during the examination and at one point had an episode of retching and gagging. Several soft subcutaneous masses were palpated in the submandibular and thoracic regions.

Diagnostics & Imaging

Hematology and serum chemistry panel results were normal. Slightly prolonged bleeding at the venipuncture site was noted after collection of the blood sample. Fine-needle aspiration cytology indicated that one of the subcutaneous masses was a hematoma. Thoracic radiography revealed increased pulmonary density and a diffuse interstitial pattern. The heart appeared normal. Coagulation testing was not performed.

Fecal Examination

Routine fecal examination had been conducted annually. Because the animal had not been tested for over a year, the client brought in a fresh fecal sample. As part of the routine fecal examination process, direct smears were conducted on all samples in addition to centrifugal fecal flotation. The direct fecal smear revealed a single motile first-stage nematode larva (L1). Because there was a high level of background debris obscuring the tail, identification of the L1 was not possible. Larvae were also detected on fecal flotation, although identification was not possible because of the adverse osmotic effects of the high specific gravity flotation media on the L1 morphology.

The direct fecal smear revealed a single motile first-stage nematode larva (L1).

Ask Yourself

1. Is fecal examination a necessary part of the baseline data in the diagnostic investigation of a dog or cat showing respiratory clinical signs?
2. What helminth parasites endemic to North America can produce respiratory signs similar to those seen in this case?
3. What parasite species should be considered when first-stage nematode larvae are detected in canine feces?

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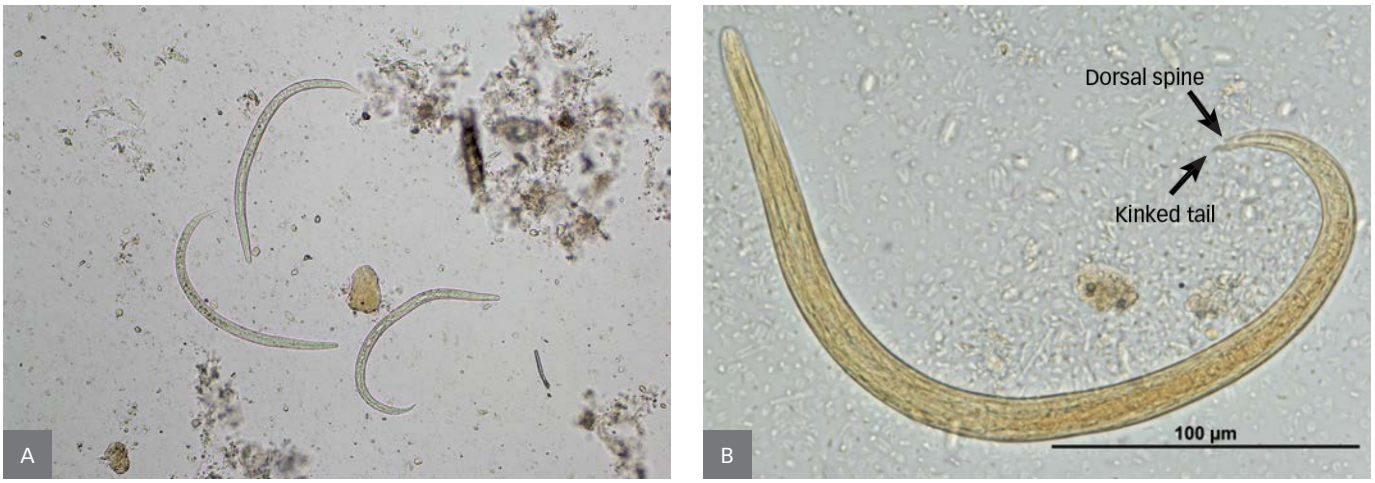

1 **(A) First-stage larvae of *A vasorum* (100× magnification). (B) Iodine-killed first-stage *A vasorum* larvae (400× magnification). Note the kinked tail and dorsal spine in the magnified view.**

Diagnosis

Angiostrongylus vasorum infection

Diagnostic Investigation

The feces was further examined by the Baermann technique, during which a large number of motile larvae were recovered (**Figure 1A**). Larvae were immobilized for detailed examination by adding a drop of dilute iodine solution (color of weak tea) to the edge of the coverslip. The larvae were about 360 microns in length, with a cephalic button at the anterior end. In addition, the length of the esophagus was almost half the length of the larvae, and the tail was kinked and contained a dorsal spine (**Figure 1B**). The size and morphology of the larvae were consistent with *A vasorum*, the French heartworm.

A vasorum is a metastrongyloid infecting the pulmonary artery and right heart of wild and domestic canids. Infection is acquired through the ingestion of infective third-stage larvae contained in the tissues of terrestrial gastropods or frogs.

Angiostrongylosis should be considered in any case of cardiorespiratory disease and/or bleeding disorders in dogs with a history of travel to known endemic regions (see ***A vasorum*: Coming to an Area Near You?**). The dog in this case was most likely infected while in Denmark, where *A vasorum* infection has become increasingly common over the past 2 decades.[1]

A vasorum infection in dogs ranges from subclinical to fatal and tends to be chronic. Clinical signs can be variable but most often are cardiorespiratory in nature. Chronic cough, dyspnea, lethargy, and exercise intolerance are commonly observed. Poorly understood bleeding disorders, suspected in this case because of hematomas, occur with some infections.[1] Sudden death can occur from fatal cerebral, thoracic, or abdominal hemorrhage. Diagnosis occurs by detection of L1 by Baermann examination of feces; fecal flotation has poor sensitivity for *A vasorum* L1.

Fecal larval shedding is erratic, resulting in the possibility of false-negative fecal examination results.[1] Therefore, at least 3 Baermann examinations should be pursued before ruling out the possibility of angiostrongylosis. Paradoxically, in more than half of the cases of natural infection, L1 can be detected by direct fecal smears, which use only a small amount of feces; this indicates high shedding levels.[4] L1 tail morphology (kinked tail, dorsal spine) is characteristic for *A vasorum*.[5]

Did You Answer?

1. Multiple species of lungworm are endemic in North America. Although lungworms are diagnosed infrequently, fecal examination (an inexpensive, noninvasive test) should be considered in cases involving signs of chronic respiratory disease in dogs or cats.
2. *A vasorum, Crenosoma vulpis, Eucoleus aerophilus, Filaroides hirthi, Oslerus osleri, Paragonimus kellicotti*
3. *C vulpis, F hirthi, O osleri, Strongyloides stercoralis*

Clinical signs can be variable but most often are cardiorespiratory in nature.

Treatment

Moxidectin, milbemycin oxime, and fenbendazole have all been used with varying degrees of success in treating dogs infected with *A vasorum*.[6] Moxidectin and milbemycin oxime given monthly (as with *Dirofilaria immitis* prevention) were reported to have 100% and 85% to 99% efficacy, respectively, in the prevention of *A vasorum* infections.[6,7]

This dog was treated with milbemycin oxime (0.5 mg/kg PO q1wk for 4 weeks).

Outcome

Cough and subcutaneous hematomas resolved within 2 weeks of the start of anthelmintic therapy. At least 3 post-treatment Baermann examinations should be conducted to monitor treatment success. Baermann examinations were negative at 1, 4, and 8 weeks after the administration of the last anthelmintic treatment, and the dog continued to do well. ■ cb

A vasorum: Coming to an Area Near You?

First reported in France, *A vasorum* appears to have been introduced into other geographic regions and currently is seen in parts of Europe, Africa, South America, and North America. In Newfoundland, *A vasorum* has been reported in dogs, red foxes, and coyotes.[1] Recently, infection was diagnosed in a red fox in West Virginia.[2] Whether this is a recent introduction or a longstanding endemic focus is unknown.

The potential spread of *A vasorum* to other parts of North America is a grave concern: Computer modeling suggests that conditions are suitable for the establishment of *A vasorum* in the eastern half and in the western coastal areas of the continent.[3]

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vetsulin®
(porcine insulin zinc suspension)

NADA 141-236, Approved by FDA

CAUTION
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATION
vetsulin® (porcine insulin zinc suspension) is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in dogs and cats with diabetes mellitus.

CONTRAINDICATIONS
Dogs and cats known to have a systemic allergy to pork or pork products should not be treated with vetsulin®. vetsulin® is contraindicated during periods of hypoglycemia.

WARNINGS
User Safety: For use in animals only. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. Accidental injection may cause clinical hypoglycemia. In case of accidental injection, seek medical attention immediately. Exposure to product may induce a local or systemic allergic reaction in sensitized individuals.

Animal Safety: Owners should be advised to observe for signs of hypoglycemia (see Owner Information Sheet). Use of this product, even at established doses, has been associated with hypoglycemia. An animal with signs of hypoglycemia should be treated immediately. Glucose should be given orally or intravenously as dictated by clinical signs. Insulin should be temporarily withheld and, subsequently, the dosage should be adjusted, if indicated. Any change in insulin should be made cautiously and only under a veterinarian's supervision. Changes in insulin strength, manufacturer, type, species (animal, human) or method of manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage.

Appropriate diagnostic tests should be performed to rule out endocrinopathies in pets that are difficult to regulate (e.g., hyperadrenocorticism in dogs and hyperthyroidism in cats).

PRECAUTIONS
Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia are essential to attain and maintain adequate glycemic control and prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies, and glucocorticoids can have an antagonistic effect on insulin activity. Intact bitches should be ovariohysterectomized. Progestogen and glucocorticoid use should be avoided.

Drug Interactions:
In the US clinical effectiveness studies, dogs and cats received various medications while being treated with vetsulin® including antimicrobials, antivirals, antifungals, antihistamines, analgesics, anesthetics/tranquilizers, diuretics, bronchodilators, corticosteroids (cats), NSAIDs, thyroid hormone supplementation, hyperthyroid medication (methimazole), internal and external parasiticides, anti-emetics, dermatological topical treatments and oral supplements, ophthalmic preparations containing antimicrobials and antiinflammatories, and various vaccines. No medication interactions were reported. This drug was not studied in dogs receiving corticosteroids.

Reproductive Safety: The safety and effectiveness of vetsulin® in breeding, pregnant, and lactating dogs and cats has not been evaluated.

Use in puppies and kittens: The safety and effectiveness of vetsulin® in puppies and kittens has not been evaluated.

ADVERSE REACTIONS
Dogs
In the field effectiveness and safety study, 66 dogs were treated with vetsulin®. Sixty-two dogs were included in the assessment of safety. Hypoglycemia (defined as blood glucose < 50 mg/dL) with or without associated clinical signs occurred in 35.5% (22/62) of the dogs at various times during the study. Clinical signs of hypoglycemia were generally mild in nature (described as weakness, lethargy, stumbling, falling down, and/or depression). Disorientation and collapse were reported less frequently and occurred in 16.1% (10/62) of the dogs. Two dogs had a seizure and one dog died during the seizure. Although never confirmed, the presumptive diagnosis was hypoglycemia-induced seizures. In the rest of the dogs, hypoglycemia resolved with appropriate therapy and adjustments in insulin dosage. Seven owners recorded the following observations about the injection site on the home monitoring forms: swollen, painful, sore, and a bleb under the skin.

The following clinical observations occurred in the field study following treatment with vetsulin® and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the dogs: hematuria, vomiting, diarrhea, pancreatitis, non-specific hepatopathy/pancreatitis, development of cataracts, and urinary tract infections.

In a 21-day field safety and effectiveness study, 40 dogs, already well controlled on vetsulin®, were administered vetsulin® using a VetPen™ insulin pen loaded with a pre-filled 2.7 mL vetsulin® cartridge and 29 gauge/12 mm pen needles. All dogs enrolled in the study were evaluated for safety. Loss of diabetic control was reported in 10 dogs, 3 of which were withdrawn from the study. Four dogs' loss of control resolved after dose adjustment while still using the insulin pen. For the remaining 3 dogs, the loss of diabetic control was reported at the end of the study and outcome was not documented. Two dogs had injection site reactions: edema in one dog and two instances of crusting in another. Poor appetite and weight loss was reported in one dog.

Cats
In a field effectiveness and safety study, safety data was reported for 78 cats receiving vetsulin®. Hypoglycemia (defined as blood glucose < 50 mg/dL) was reported in 61 cats (88 total incidences). Fifteen of the occurrences (involving 13 cats) were associated with clinical signs described as lethargy, diarrhea, decreased appetite/anorexia, vomiting, and hypothermia. One cat had seizures following accidental overdosing by the owner and again during the subsequent dose adjustment period. The cat responded to supportive therapy and had no further hypoglycemic episodes. In all cases of hypoglycemia, the clinical signs resolved following symptomatic treatment and/or dose adjustment. Polyneuropathy was reported in 4 cats. Two injection site reactions were reported: one as a mildly thickened subcutaneous tissue reaction and the second as a mild bruising.

The following clinical observations occurred in the field study following treatment with vetsulin® and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the cats: vomiting, lethargy, diarrhea, decreased appetite/anorexia, pancreatitis, dermal events, respiratory disease, urinary tract disorder, renal disease, dehydration, weight loss, polydipsia, polyuria, behavioral change, and ocular discharge/conjunctivitis. In a smaller field effectiveness and safety study, 14 cats were treated with vetsulin®. Hypoglycemia was reported in 6 cats (8 total occurrences). Lethargy not associated with hypoglycemia was reported in 4 cats (6 total occurrences). The following clinical observations occurred in the field study following treatment with vetsulin® and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the cats: foul odor to stool, diarrhea, dull coat, rapid, shallow breathing, stiff gait in rear, gallop rhythm, and pruritus with alopecia.

During the 1998–2007 period, the following adverse events in 50 cats treated with porcine insulin zinc suspension were reported to Intervet International and Intervet Inc: Death, seizures, lack of effectiveness/dysregulation, hypoglycemia, allergic or skin reaction, lethargy, vomiting/diarrhea, injection pain, hyperthermia, nystagmus, PU/PD, and abnormal behavior.

In a 21-day field safety and effectiveness study, 36 cats, already well controlled on vetsulin®, were administered vetsulin® using a VetPen™ insulin pen loaded with a pre-filled 2.7 mL vetsulin® cartridge and 29 gauge/12 mm pen needles. Loss of diabetic control was reported in three cats all of which resolved after dose adjustment while still using the insulin pen. Hypoglycemia was reported in one cat. The cat recovered with supportive care and dose adjustment.

To report suspected adverse drug experiences, call Merck at 1-800-224-5318.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or http://www.fda.gov/AnimalVeterinary/SafetyHealth

Use contents within 42 days of first puncture.
Supplied: 10 ml vial and 2.7 cartridge

Additional information about vetsulin®, VetPen™, and diabetes mellitus can be found at www.vetsulin.com

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