

Anaphylactoid reaction in a heartworm-infected dog undergoing lung lobectomy

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Case Description—A 7-year-old 23-kg (50.6-lb) spayed female Border Collie with a history of heartworm disease was evaluated for respiratory distress.

Clinical Findings—Computed tomography of the thorax revealed possible pulmonary bullae or blebs, and on the basis of these findings, a tentative diagnosis of bullous emphysema was made.

Treatment and Outcome—Exploratory median sternotomy revealed gross pathological lesions in the right caudal lung lobe; the most peripheral portion appeared discolored (pale pink), and a clear line of demarcation was observed. Upon excision of the affected lung lobe, a worm segment was noticed both on the remaining stump of the lung lobe in the dog and in the removed lobe. At this time, the dog had an anaphylactoid reaction. The reaction was successfully treated with fluid therapy, antihistamines, and corticosteroids. Lung lobectomy of the right caudal lobe resulted in clinical resolution of the bilateral pneumothorax. However, during the postoperative period, the dog developed a hemothorax and was returned to surgery. As no obvious cause for the hemothorax was seen at the second surgery, the dog was treated for a potential coagulopathy with fresh frozen plasma, which provided clinical resolution of the hemothorax. Parasitological examination of the worm segment confirmed a *Dirofilaria immitis* infection. The dog was discharged 5 days after surgery and treated with doxycycline for 30 days and monthly administration of heartworm preventative was prescribed.

Clinical Relevance—Heartworm infection should be a differential diagnosis in dogs with spontaneous pneumothorax. Anaphylactoid reactions associated with accidental dissection of adult heartworms should be managed with treatment aimed at cardiovascular stabilization. (*J Am Vet Med Assoc* 2011;238:1301–1304)

A 7-year-old 23-kg (50.6-lb) spayed female Border Collie was evaluated by the emergency service of the Veterinary Teaching Hospital at North Carolina State University College of Veterinary Medicine for respiratory distress secondary to bilateral pneumothorax. The dog had a history of positive heartworm test results 2 years previously, and although no adulticide treatment was given, the dog had been receiving monthly administration of heartworm preventative^a since the owner adopted it 18 months ago. The dog had no history of trauma. Earlier that day, the owner noticed that the dog vomited its morning meal and began to have marked respiratory distress and concurrent signs of anxiety. The dog was taken to the referring veterinarian, and a dorsoventral radiographic image of the thorax revealed bilateral pneumothorax. The referring veterinarian performed a left-sided thoracocentesis, and removed 2 L of air; however, negative pressure could not be achieved. The dog was referred for ongoing further diagnostic evaluation and management.

Upon arrival at the hospital, the dog was bright, alert, and responsive. The HR was 120 beats/min with normal pulses, and no murmur was auscultated. The

ABBREVIATIONS

HR	Heart rate
MAP	Mean arterial pressure
PT	Prothrombin time

dog was panting, and on thoracic auscultation, lung sounds were considered quieter than normal bilaterally in the dorsal fields. The remainder of the physical examination was unremarkable. A catheter was placed in the right cephalic vein, and a sample of venous blood was obtained for assessment of PCV, total protein concentration, CBC, serum biochemical analysis, and a heartworm antigen ELISA.^b The only abnormality found on CBC was mild leukocytosis (12.84×10^3 cells/ μ L; reference range, 4.39×10^3 cells/ μ L to 11.61×10^3 cells/ μ L) characterized by mild neutrophilia (11.042×10^3 cells/ μ L; reference range, 2.84×10^3 cells/ μ L to 9.11×10^3 cells/ μ L). Serum biochemical analysis revealed mildly increased albumin concentration (4.3 g/dL; reference range, 3.0 to 3.9 g/dL) and alanine transaminase activity (114 U/L; reference range, 12 to 54 U/L). Results of the heartworm test were positive and indicated a high serum antigen concentration. The dog was sedated with butorphanol (0.3 mg/kg [0.14 mg/lb], IV) and acepromazine (0.02 mg/kg [0.009 mg/lb], IV), and two 14-gauge fenestrated polyurethane catheters^c were inserted, one on each hemithorax. Initially, 195 mL of air was aspirated from the right hemithorax and 470 mL of air was aspirated from the left hemithorax. The dog was connected to a continuous chest tube drainage system^d

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for overnight management. Thoracic radiographs were obtained and showed continued evidence of bilateral pneumothorax; however, pneumothorax was noted as considerably improved, compared with its appearance on the radiograph from the referring veterinarian.

The dog was anesthetized the next day for diagnostic imaging via helical computed tomography. On preanesthetic evaluation, the dog was bright, alert, and responsive, and the dog's physical status was classified as a 3 (a patient with severe systemic disease), according to the scheme adopted by the American Society of Anesthesiologists.¹ The dog was premedicated with acepromazine (0.01 mg/kg [0.005 mg/lb], IV) and buprenorphine (0.01 mg/kg, IV), and anesthesia was induced with propofol (3.6 mg/kg [1.64 mg/lb]). Anesthesia was maintained with isoflurane (1% to 2%) in oxygen, and the dog was allowed to breathe spontaneously. The total anesthetic time was 1 hour 20 minutes, during which time HR, respiratory rate, systolic arterial pressure, MAP, diastolic arterial pressure, SpO₂, end-tidal CO₂ concentration, and rectal temperature were monitored and remained within clinically acceptable limits. The computed tomographic scan revealed continued mild bilateral pneumothorax as well as possible pulmonary blebs in the medial aspect of the cranial lung lobes. Anesthetic recovery was unremarkable, and the dog was returned to the intensive care unit for continued monitoring.

The dog was anesthetized again the following day for a thoracic exploration via a median sternotomy. On preanesthetic evaluation, the dog was again bright, alert, and responsive; however, it was noted that the right-sided chest tube was no longer functional. Breath sounds could be auscultated throughout all lung fields bilaterally. The dog's physical status was again classified as a 3, according to the scheme adopted by the American Society of Anesthesiologists.¹ The dog was premedicated with hydromorphone (0.1 mg/kg [0.05 mg/lb], IV), and anesthesia was induced with propofol (4.4 mg/kg [2.0 mg/lb]). Anesthesia was maintained with isoflurane (1.5% to 3.5%) and a continuous rate infusion of fentanyl (0.3 to 0.5 µg/kg/min [0.14 to 0.23 µg/lb/min]). A 20-gauge catheter was placed in the dorsal pedal artery, and direct arterial blood pressure monitoring was performed. The patient was mechanically ventilated on a positive pressure ventilator,^e and anesthesia was unremarkable for the initial 3 hours. A median sternotomy was performed, and the lung lobes were visually inspected for leakage or the presence of bullae or blebs. Although no bleb or bulla was found and no bubbles were observed after sequential immersion of the lung lobes, the right caudal lobe was noted to appear abnormal. The most peripheral portion appeared discolored (pale pink), and a clear line of demarcation was observed. Positive pressure could not deploy alveoli in this area, although the rest of the lung lobes were fully inflated (maximum inflation pressure, 20 cm H₂O). In the absence of any other finding, it was hypothesized that this abnormal portion of the lung could represent an area of suspicious potential leakage. At this time, the dog's HR was 70 beats/min and MAP was 85 mm Hg. A right lung lobectomy was performed by stapling and removal of the right caudal lung lobe

near the hilus with a stapling device.^f A worm segment was observed both on the remaining stump of the lung lobe and on the cut surface of the lobe as it was placed into formalin.

At this time, the dog became acutely tachycardic (HR, 180 beats/min) and hypotensive (MAP, 38 mm Hg). The anesthetist began initial treatment for presumed bleeding and summoned an anesthesiologist. A 15 mL/kg (6.8 mL/lb) bolus of lactated Ringer's solution was administered with no change in either HR or MAP. The thorax was evaluated for potential bleeding, but none was found. Administration of crystalloid fluids was continued at bolus rate for a total of 22 mL/kg (10 mL/lb), and phenylephrine (2.0 µg/kg [0.9 µg/lb], IV) was administered. There was a minimal response to the phenylephrine, with the HR decreasing to 150 beats/min and MAP increasing to 45 mm Hg; therefore, the phenylephrine dose was repeated. The second dose produced no change in HR; however, MAP increased to 62 mm Hg. At this time, the anesthesiologist, who had not been in the room at the time the lung lobe was removed, questioned the surgeon as to whether anything unusual had occurred and was informed about the worm. Diphenhydramine (1 mg/kg [0.45 mg/lb], IV) and dexamethasone sodium phosphate (0.15 mg/kg [0.07 mg/lb], IV) were administered, resulting in resolution of the tachycardia and stabilization of blood pressure. Within 10 minutes of the final drug administrations, the HR had returned to 92 beats/min and MAP had risen to 75 mm Hg. The period of anaphylaxis lasted for approximately 25 minutes, and anesthesia was unremarkable for the remaining 45 minutes of the procedure and recovery.

Following anesthetic recovery, the dog was admitted to the intensive care unit for monitoring and postoperative care. Over the subsequent 2 hours, 375 mL of blood was aspirated from the chest tubes. The PCV of the aspirated fluid was determined to be 15% at 1 hour and 40% at 2 hours with a peripheral PCV of 37%. A PT of 17 seconds (reference range, 9 to 12 seconds) and partial thromboplastin time of 84 seconds (reference range, 59 to 87 seconds) were recorded, and the dog received an autotransfusion of 100 mL of the blood recovered from the chest tube. In the face of massive blood loss, the mild increase in PT and normal partial thromboplastin time were not regarded as good indicators of the patient's current physical status, and the dog was started on a transfusion of fresh frozen plasma (190 mL total) and sent back to the surgical suite. During reexploration of the chest cavity, no major bleeding vessels were found, but suspicious areas were double ligated in the area of the internal thoracic arteries on both sides of the sternum. The lung lobectomy site was examined, and no clot or leakage was seen. The anesthesia and subsequent anesthetic recovery were unremarkable. After the second surgery, the dog made an uneventful recovery. After surgery, the chest tube was aspirated intermittently and produced moderate volumes of serosanguineous fluid. The tube was removed at 63 hours after surgery.

Histologic examination of the submitted lung lobe revealed severe atelectasis with mild peribronchiolar and perivascular lymphocytic cuffing as well as mu-

cus, eosinophils, and macrophages in the bronchi and bronchioles. This was indicative of a low-grade inflammatory process; however, no evidence of parasitic disease was observed, likely attributable to long-term heartworm preventive treatment. A parasitological evaluation of the worm segment removed from the dog confirmed the diagnosis of infection with *Dirofilaria immitis*. The dog was discharged 5 days after surgery and received doxycycline (4.4 mg/kg, PO, q 12 h) for 30 days as well as continued monthly administration of heartworm preventative.^a

Discussion

This case report illustrates several important points regarding identification of risks and management of dogs with positive heartworm test results. To the authors' knowledge, this is the first report of an anaphylactoid reaction caused by surgical dissection of the *Dirofilaria immitis* organism during lung lobectomy.

The prevalence of *D immitis* infections in dogs varies according to geography; however, spontaneous pneumothorax secondary to heartworms has been described in both dogs and cats.²⁻⁴ As such, heartworm infection should be a differential diagnosis in patients with spontaneous pneumothorax, particularly in endemic regions. The exact mechanism by which heartworm disease can lead to pulmonary blebs or bullae is unknown; however, several theories have been proposed. Death of adult worms can lead to thrombosis in peripheral pulmonary arteries,⁵ and subsequent ischemia could lead to rupture of alveoli. In addition, pneumothorax secondary to pulmonary hypertension or secondary bacterial abscesses have been suggested.² Although this dog was known to have a positive heartworm test result previously, diagnostic imaging suggested that the presence of pulmonary blebs and bullous emphysema was assumed.

Anaphylactoid reactions attributed to *D immitis* have been described anecdotally in both dogs and cats but are not fully understood. This reaction has been attributed to parasite death and has been hypothesized to result from exposure to the cuticle of the worm.⁶ Anaphylactoid reactions can lead to shock and circulatory collapse. There are many different types of shock, subdivided by clinical and clinicopathologic differences, and several studies have been performed to determine the type of shock associated with heartworm disease. A study⁷ evaluating serum concentrations of tumor necrosis factor, a mediator of endotoxic shock, in dogs receiving heartworm extract IV demonstrated only a minimal and late increase in tumor necrosis factor concentration. Tumor necrosis factor concentrations increase dramatically and rapidly with endotoxic shock; therefore, it was determined that the mechanism of heartworm extract-induced shock was unlikely to be the same as endotoxic shock.⁷ In another study,⁸ heartworm extract was administered to dogs to evaluate plasma histamine concentrations. Histamine secondary to mast cell degranulation is an important mediator in anaphylactic shock. The study showed varying plasma concentrations of histamine at the onset of shock, indicating the effect of other factors. In addition, investigators in that study⁸ noted that an unknown substance

contained in the heartworm extract precipitated mast cell degranulation, a phenomenon previously described for some drugs and chemicals.^{9,10} As the exact mechanism of the anaphylactoid reaction is not understood, treatment has been aimed at resolution of shock. Anecdotal suggestions of treatment include antihistamine drugs for presumed mast cell degranulation as well as epinephrine for anaphylaxis; however, no standard-of-care guidelines exist. In this dog, treatment with diphenhydramine, an antihistamine, and an anti-inflammatory dose of corticosteroids resolved the cardiopulmonary effects of the anaphylactoid reaction.

An interesting factor in this dog was the presumed coagulopathy that developed in the postoperative period. Unfortunately, a full coagulation profile was not obtained, but the PT from the point-of-care device was mildly increased, potentially implying an effect of the heartworm on the extrinsic coagulation pathway. In one study,¹¹ heartworm extract was administered IV to dogs, and coagulation profiles were obtained after the onset of clinical shock. Investigators in that study demonstrated increases in both PT and partial thromboplastin time in 1 group and surmised coagulopathy could arise from heartworm extract-inhibited activation of coagulation factors. In that study, investigators also successfully treated the prolonged PT in vitro by the administration of plasma from clinically normal dogs, potentially supporting the resolution of the bleeding in the patient of the present report after treatment with fresh-frozen plasma. Another potential cause of coagulopathy that cannot be ruled out is thrombocytopenia secondary to the anaphylactoid reaction during surgery. A decrease in platelet count has been described secondary to IV administration of heartworm extract.¹² However, this is less likely, as resolution of the clinical bleeding occurred with plasma administration and a second surgical procedure, neither of which would be expected to improve the platelet count. An additional consideration regarding the presumed coagulopathy is the effect of several of the drugs that the dog received in the perioperative period. Propofol is reported to decrease platelet aggregation in humans; however, bleeding time is not affected, and the clinical importance of this finding is therefore questionable.¹³

In conclusion, *D immitis* infection should always be considered in dogs with spontaneous pneumothorax. In patients with confirmed or suspected infection, care should be taken not to inadvertently dissect a worm, and if signs of an anaphylactoid reaction occur, treatment should be aimed at cardiovascular stabilization. In addition, the possibility of subsequent coagulopathy should be considered, and treatment should be instituted when necessary.

- a. Heartgard, Merial Ltd, Duluth, Ga.
- b. SNAP, Idexx, Westbrook, Me.
- c. MILA International Inc, Erlanger, Ky.
- d. Argyle Thora-Seal III, Tyco, Mansfield, Mass.
- e. Hallowell Model 2000, Hallowell EMC, Pittsfield, Mass.
- f. Thoracoabdominal 90-mm stapler, Ethicon Inc, Somerville, NJ.

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From this month's AJVR

Effect of duration and type of anesthetic on tear production in dogs

Molly K. Shepard et al

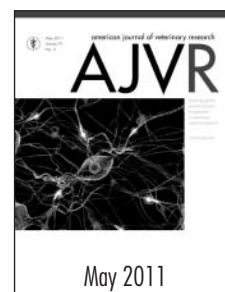
Objective—To determine effects of duration and type of anesthetic on tear production in dogs.

Animals—8 female Beagles.

Procedures—Each dog was randomly allocated into 1 of 4 groups according to a Latin square design to receive anesthesia as follows: 1 hour with isoflurane, 1 hour with desflurane, 4 hours with isoflurane, and 4 hours with desflurane. Each dog was anesthetized with the selected inhalant 4 times during a 4-week period, with at least 5 days separating anesthetic episodes. Aqueous tear production was measured via the Schirmer I tear test at baseline and 10 minutes, 30 minutes, and 1 hour after induction of anesthesia as well as 2, 3, and 4 hours after induction for the 4-hour groups. Tear production was also measured after the dogs were standing after recovery from anesthesia and 2, 10, and 22 hours after recovery from anesthesia.

Results—Aqueous tear production was significantly reduced in dogs during anesthesia and returned to baseline values immediately after recovery and until 10 hours after anesthesia in all treatment groups. Inhalant type and duration had no significant effect. Neither lateral recumbency nor left versus right eyes had a significant effect.

Conclusions and Clinical Relevance—Results suggested that inhalant anesthetics did not reduce tear production after anesthesia and that longer-duration anesthesia did not cause decreased tear production, compared with shorter-duration anesthesia. (*Am J Vet Res* 2011;72:608–612)



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