

**Date Patient Admitted**

February 19, 2015

**Patient Name and ID#**

Barney (ID# - 313187)

**Patient Signalment**

Canine, Shih Tzu, M/N, 4 years old

**Patient History**

Barney presented to the emergency service at the Tufts Cummings School of Veterinary Medicine for evaluation of heartworm disease (*Dirofilaria immitis* (*d. immits*)) and heartworm embolectomy. Barney was adopted from a shelter in South Carolina in March 2014. At that time, he tested heartworm positive on a monoclonal antibody-based ELISA test. Barney was receiving monthly PO ivermectin/pyrantel (Tri-Heart Plus® 0-25 lbs) and topical flea and tick preventative. Barney's owners noticed that his urine was discolored after urinating on the snow. They brought him to his primary care veterinarian where they performed a CBC, chemistry profile, and urinalysis (UA). Results showed evidence of mild anemia and hemoglobinuria. Barney was taken to a referral hospital in South Carolina for further workup. An echocardiogram was performed that showed heartworms in Barney's right heart and pulmonary artery (PA). He was started on doxycycline 7.3 mg/kg (50 mg) PO BID and then referred for heartworm embolectomy.

### **Patient Status upon Presentation**

On physical examination, Barney was bright, alert, and responsive (BAR). He weighed 6.8 kg with a 5 out of 9 body condition score; Temperature (T) was 101.6°F, heart rate (HR) was 100 bpm with a respiratory rate (RR) of 40 breaths per minute (breaths/min) and normal bronchovesicular sounds heard bilaterally. His mucous membranes (MM) were light pink and mildly tacky suggestive of dehydration, anemia, or decrease in cardiovascular perfusion. There was no jugular venous distention. His pulse quality was good.

On cardiac auscultation, there was a grade II-III/VI systolic and diastolic left basilar murmur and a V/VI diastolic right basilar murmur with a palpable precordial thrill.

### **Problem List**

The problem list included caval syndrome; grade II-III/VI systolic and diastolic left basilar murmur; V/VI diastolic right basilar murmur.

### **Differential Diagnosis**

The differential diagnosis included severe heartworm disease resulting in caval syndrome.

### **Initial Assessment of Prognosis**

Barney's owners were given a guarded prognosis. If left untreated, risk of mortality would increase, clinical signs would worsen, and he would develop right-sided congestive heart failure (CHF).

### **Initial Diagnostics and Results**

A CBC, serum biochemical profile, and UA were performed prior to arrival. UA revealed proteinuria >500 mg/dL, hematuria/hemoglobinuria, and bilirubinuria. Proteinuria is common with severe and chronic heartworm infection leading to immune-complex glomerulonephritis.

Hemoglobinuria and bilirubinuria are associated with intravascular hemolysis of the red blood cells from the presence of heavy worm burden. There was no microfilaria seen on his CBC. His Hct was 37.7%. He had an increased reticulocyte count at 166 K/uL, which was likely secondary to hemolysis causing anemia or just a transient physiologic response to increased peripheral demand. Serum biochemical profile was within normal limits except for mild hyperglobulinemia at 4.3 g/dL, a common finding in chronic heartworm disease due to chronic antigenic stimulation.

Upon arrival to the emergency service, an IV catheter was placed and a Nova® biomedical Stat Profile® pHOx® Ultra (Nova®) and UA were submitted. His PCV was 40% and had a mildly elevated total solids (TS) of 7.8 g/dL. His Nova® revealed mild hypoglycemia at 78 mg/dL and mild hypermagnesemia at 0.5 mmol/L. His UA showed no hematuria; however, hemoglobinuria and proteinuria were still present.

Thoracic radiographs revealed an enlarged and tortuous PA and generalized cardiomegaly.

Echocardiogram showed numerous heartworms in his right heart and PA, visualized as double-lined echogenic densities. There was also right ventricular (RV) concentric hypertrophy and cavity dilation, left ventricular (LV) concentric hypertrophy and small LV cavity, dilation of the main PA, and systolic flattening of the interventricular septum that was consistent with RV pressure overload. Color flow (CF) Doppler revealed pulmonic insufficiency (PI) and tricuspid regurgitation (TR) that were secondary to heavy worm burden in the main PA, RV and RA obstructing the tricuspid valve (TV) and pulmonic valve apparatus. Using the modified Bernoulli equation ( $\text{pressure} = 4 \times \text{velocity}^2$ ), RV systolic pressure can be measured. Unfortunately, the abundance of worms in his right heart made it difficult to obtain a TR velocity. The pulmonic

flow profile can be used to assess severity of pulmonary hypertension (PHT), and in Barney's case, his profile showed a rapid acceleration and mid to late systolic notching during deceleration, consistent with severe PHT.

Barney's clinical signs and diagnostic tests were consistent with caval syndrome secondary to severe heartworm disease. Barney's owners were notified of the risks associated with the heartworm extraction procedure, which included anaphylaxis and pulmonary vasoconstriction from release of worm antigen and worm emboli from manipulation of the worms during the procedure.

### ***Medications***

- Dexamethasone sodium phosphate (SP) 2.94 mg/kg (20 mg) was administered IV, slowly over 30 minutes prior to procedure. Pretreatment with corticosteroids prior to heartworm removal helps reduce inflammation associated with pulmonary thromboembolism.
- Cefazolin 22 mg/kg (138 mg) IV was administered at the start of the procedure, then every 90 minutes. Prophylactic antibiotic use during surgery is helpful in reducing incidence of infection.
- Unfractionated heparin at 100 IU/kg (680 IU) IV was also administered at the start of the procedure. Heparin helps reduce the severity of pulmonary thrombosis, improving blood flow, inhibiting fibrin production, reducing platelet consumption, red cell damage, hemolysis, anemia and hemoglobinuria.

### ***Treatments***

- RR and effort monitoring q1h; NPO; walk and monitor for hematuria/hemoglobinuria q4h

Barney had a preanesthetic workup performed by a board-certified anesthesiologist and an anesthesia veterinary technician specialist. He was administered 0.10 mg/kg (0.7 mg)

hydromorphone and 0.19 mg/kg (1.3 mg) midazolam IV as a preanesthetic medication. Barney was induced with 4.41 mg/kg (30 mg) propofol IV, intubated, and maintained on isoflurane inhalant. He was carefully monitored by the anesthesia service. IV fluids were administered during the procedure to help improve cardiac output.

Barney was placed in left lateral recumbency. The right cervical region was clipped and prepped with aseptic technique. Using a #10 blade, the skin was incised over the right jugular vein, and the jugular vein was then isolated using blunt dissection. A ligature was placed around the proximal and distal ends of the jugular vein to control bleeding. Once secured, a small incision was made in the jugular vein through which Ishihara forceps were inserted to extract the heartworms. Carefully, the forceps were advanced repeatedly into the cranial vena cava, RA, and RV to remove heartworms under fluoroscopic and transesophageal echocardiographic guidance. Seventeen intact worms (11 females and 6 males) were extracted. Additional attempts were made to extract the remaining heartworms seen on transesophageal echocardiogram. Short runs of ventricular tachycardia were seen with manipulation of the Ishihara forceps within the RV. After 5 unsuccessful attempts to remove the heartworms, the procedure concluded. The right jugular vein was repaired, and the incision was sutured closed. A lightly padded bandage was placed around Barney's neck to cover his incision.

### ***Medications Post-op***

- Cefazolin sodium 22 mg/kg (150 mg) IV TID
- Doxycycline 7.9 mg/kg (50 mg) PO BID. Doxycycline is used to eliminate *Wolbachia* sp., an intracellular Gram-negative bacterium that contributes to the inflammatory response by releasing endotoxins and antigens associated with worm death.

### ***Treatments Post-Op***

- Incision monitoring (hemorrhage, swelling, bruising) q1h for the first 4 hours, then q4h
- HR monitoring q1h for the first 6 hours, then q4h
- RR and effort monitoring q1h for the first 6 hours, then q4h
- Temperature check q1h until greater than 100°F
- MM color and CRT q1h for the first 6 hours, then q4h
- IV catheter care and flush q4h
- Walk and monitor for hematuria/hemoglobinuria q4h
- Feed and monitor appetite q12h; provide water q4h

### **Daily SOAP Notes – Day 1 (Discharge)**

#### ***Subjective***

Barney was BAR; mild tachypnea at rest

#### ***Objective***

Wt: 6.8kg; T:101.6°F; HR: 100 bpm; RR: 36-44 breaths/min; normal bronchovesicular sounds heard bilaterally. MM were pink with CRT <2s; grade II-III/VI diastolic right basilar murmur was auscultated; neck bandage clean; incision intact and healing properly; great appetite and drinking well; no visible hematuria or hemoglobinuria on urination.

#### ***Medications***

- Discontinued cefazolin
- Doxycycline (7.4 mg/kg) 50 mg capsules PO BID

#### ***Treatments***

- Change neck bandage prior to discharge
- Incision monitoring (hemorrhage, swelling, bruising) q4h

- HR monitoring q6h
- RR and effort monitoring q1h
- MM color and CRT q4h
- Removed IV catheter
- Walk and monitor for hematuria/hemoglobinuria q4h
- Feed and monitor appetite q6h; provide water q4h

### ***Assessment***

A recheck echocardiogram was performed which revealed no heartworms in the RV and RA; however, at least two heartworms were present in the PA. Using CF Doppler, there was still TR and PI. The cause of his diastolic murmur was secondary to severe PI. His mild tachypnea could be the result of antigen release from worm removal, pulmonary thromboembolism, or possibly from mild discomfort from his incision or anxiety. A recheck PCV, TS, BG, and Azostick® were within normal limits. A free catch urine sample revealed cloudy, dark yellow urine with 1+ bilirubin and protein, which was expected to resolve within the next 24 to 48 hours.

### ***Plan***

If Barney was breathing comfortably with an improved RR, he would be discharged that evening into the care of the owners.

### **Final Outcome**

Barney was breathing comfortably towards the end of his stay and was discharged into the care of his owners. His owners were given instructions for exercise restriction and incisional care. Strict exercise restriction will minimize cardiac output and pulmonary blood flow, which puts strain on the RV, increasing the risk of pulmonary thrombosis. A harness was recommended

to replace his neck collar until the neck incision was completely healed. Incision should be monitored for signs of inflammation, swelling, pain, or discharge. Sutures would need to be removed in 10-14 days. His owners were shown how to monitor his RR and effort and for any shortness of breath and coughing, as these could be signs for pulmonary thromboembolism. Barney would continue doxycycline for an additional 30 days and monthly PO ivermectin/pyrantel. Barney was to come back in one month to start adulticide treatment protocol with melarsomine.

On his one month recheck, he had a II/VI systolic left basilar ejection murmur. No diastolic murmur was heard. On recheck echocardiogram, there were still visible heartworms seen in the main PA but none in the RV or RA. He had significantly less TR and PI on CF Doppler. Thoracic radiographs revealed resolving PA enlargement. Barney still tested positive on ELISA antigen test. Barney's hematuria and hemoglobinuria resolved a couple days after discharge. He did well with the first 2.5 mg/kg (17 mg) deep IM dose of melarsomine and would return in one month for two more doses that would be given 24 hours apart.

### **Case Discussion**

Heartworm disease is a common parasitic disease in dogs. *D. immitis*, one of many filarial parasites, is a large, string like parasite that resides within the PA but may also be found in the right heart. Adult heartworms can live up to 5-7 years. Adults are 1 to 2 mm in diameter; males are 150-180 mm long with a spirally coiled caudal end; females are 250-300 mm in length. They produce microfilaria that can survive up to 2 years circulating in the blood stream. The life cycle of *D. immitis* starts when a female mosquito bites an infected host, ingesting microfilaria (L<sub>1</sub>). The L<sub>1</sub> microfilaria will mature to a L<sub>3</sub> microfilaria within the mosquito. The molt to L<sub>2</sub> occurs about 10 days after ingestion and molt to L<sub>3</sub> occurs about 13 days after ingestion. When the

mosquito bites another dog, the infective L<sub>3</sub> larvae are transmitted to the new host. The larvae penetrate into the SC tissue and molt for 50-70 days to become L<sub>4</sub> larvae. In another 4-5 months, the larvae develop into L<sub>5</sub> adults. Heartworm preventative is beneficial during this SC phase of infection. Microfilaria must be differentiated from *Acanthocheilonema reconditum* that is a nonpathogenic filarial living in SC tissues transmitted by fleas. They can be differentiated by their progressive movement, blunt head, and curved tail.

Heartworm numbers, host immune response, duration of infection, and host activity level determines the severity of the infection. Classification of heartworm disease is based on the severity of clinical signs: **Class I:** asymptomatic or mild disease; **Class II:** mild to moderate symptoms; **Class III:** severe symptoms (cough, hemoptysis, weight loss, lethargy, exercise intolerance, dyspnea, right-sided CHF); **Class IV:** caval syndrome.

Caval syndrome is an acute manifestation of heartworm disease associated with a large number of heartworms in the right heart and that encircles around and passes through the TV apparatus. The key components of the syndrome are TR with poor cardiac output and intravascular hemolysis resulting in hemoglobinemia and hemoglobinuria. Once the worms are in the RV, they can migrate to the RA by attaching to the tricuspid apparatus and pulling themselves into the RA. When there is enough pulmonary hypertension, the TR will become severe enough that it decreases forward blood flow through the pulmonary vasculature and left heart, resulting in left heart volume depleted or volume-underload, along with decreasing LV forward cardiac output. Poor perfusion is a result of decrease systemic blood flow. Pulmonary circulatory pressures are maintained at a level lower than systemic pressure to reduce workload of the RV. RV overload included RV concentric hypertrophy and dilation, dilation of the main PA.

Physical examination and clinical signs are variable from no clinical signs to severe disease. Cough can be due to an inflammatory disease process from the heartworms. Progressive disease severity leads to exercise intolerance, dyspnea on exertion, and signs of right-sided CHF. The diagnosis of caval syndrome is based on clinical signs, a positive heartworm antigen test and an echocardiogram confirming the presence of heartworms in the RV, RA, and PA with right sided overload

Barney's case demonstrated the presentation, treatment and management of caval syndrome secondary to heartworm infection.

### **References**

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Jr. Smith, FWK, Tilley, LP, Oyama, MA, Sleeper, MM: *Manual of Canine and Feline Cardiology, 5<sup>th</sup> Edition*, St. Louis, 2016, Elsevier