

SEVERE HEARTWORM DISEASE WITH PULMONARY HYPERTENSION IN A LOCAL DOG

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SUMMARY

A 4-year-old, male local dog was referred to University Veterinary Hospital-Universiti Putra Malaysia (UVH-UPM) due to dyspnoea and ascites. Full diagnostic investigations inclusive of blood haematology, serum biochemistry, blood smear examinations for haemopathogens, heartworm antigen test, thoracic and abdominal radiography and echocardiography were conducted. A diagnosis of severe heartworm disease was made from the positive heartworm antigen test, the presence of heartworms on echocardiography and the accompanying advanced clinical findings. This was the first case of right-sided heart failure due to severe heartworm disease with concurrent pulmonary hypertension diagnosed in UVH-UPM from which the moribund dog was successfully stabilised during hospitalisation.

Key words: Severe heartworm disease, pulmonary hypertension, right-sided heart failure

INTRODUCTION

Canine heartworm disease (CHWD) or dirofilariasis is caused by a filarial nematode known as *Dirofilaria immitis* which resides in the pulmonary arteries and occasionally in the right heart chambers of the infected dogs (Grandi *et al.*, 2010). Transmitted by mosquitoes that ingest blood, the worms cause severe lung pathologies (i.e. endarteritis and muscular hypertrophy of arteriolar walls) and morbidity in the dogs, as well as shorten their life expectancy and can cause acute disease and death (Bowman and Atkins, 2009).

CASE REPORT

A 4-year-old, male local dog was presented to University Veterinary Hospital-Universiti Putra Malaysia (UVH-UPM) due to abdominal distension, haematemesis, melena, and inappetance. Prior presentation to UVH, the dog was treated by a private veterinarian with doxycycline, amoxicillin-clavulanate, Liv-52 and folic acid for about 2 weeks, without a specific diagnosis nor the dog show clinical improvement. In contrast, the abdomen became more distended, and gastrointestinal signs such as melena and haematemesis developed.

Upon physical examination, the dog was dull, depressed, and 7% dehydrated. Other findings noted were tachypnoea, coughing and petechiation of the buccal mucosa. Lung crackles, as well as systolic heart murmur of grade IV/VI at the left and right heart bases were auscultated, which indicated pulmonic and tricuspid regurgitations, respectively. The dog was first stabilised before diagnostic workup was carried out. The tachypnoeic dog was provided with supplemental oxygen. Prior to intravenous access, furosemide (2 mg/kg, IM; Frusemide, Troy Laboratories Pty. Ltd, Australia) as a diuretic agent and tramadol hydrochloride (5 mg/kg, SC; Acugesic, CCM Duopharma Biotech, Malaysia), as an

antitussive agent were administered. The average systemic blood pressure was recorded normal on several readings. A series of diagnostic tests inclusive of haematology and serum biochemistry analyses, urinalysis, blood smear examination for haemopathogens, chest and abdominal radiography, echocardiography and heartworm antigen test (Heska®) were carried out when the dog was stabilised.

Complete blood count (Table 1) revealed non-responsive anaemia, thrombocytopenia, marked neutrophilia with a left shift and monocytosis consistent with chronic inflammation. Serum biochemistry analysis revealed azotemia most likely pre-renal in origin due to dehydration, hyperproteinaemia, and elevated ALT and ALP. Urinalysis results were unremarkable.

Table 1. Haematology and serum biochemistry values for the dog (at first presentation and two weeks after being discharged from UVH-UPM).

Parameters	Day-1	Day-14	Normal range
RBC ($\times 10^{12}/L$)	3.5	4.4	5.5-8.5
Haemoglobin (g/L)	88.0	108	120.0-180.0
PCV (L/L)	0.21	0.26	0.35-0.55
Thrombocytes ($\times 10^9/L$)	163.0	519.	200.0-500.0
Neutrophils ($\times 10^9/L$)	33.4	21.4	6.0-17.0
Band Neutrophils ($\times 10^9/L$)	1.0	1.0	< 0.3
Monocytes ($\times 10^9/L$)	1.7	1.7	0.2-1.4
Urea (mmol/L)	13.9	15.9	3.0-7.5
Creatinine (mmol/L)	108.0	91.0	88.0-176.0
Total protein (g/L)	82.3	72.2	55.0-75.0
ALT (U/L)	171.3	66.9	5.0-90.0
ALP (U/L)	190.0	159.0	40.0-100.0

Day-1, day-1 hospitalisation; Day-14, day-14 post treatment; RBC, red blood cells; PCV, packed cell volume; ALT, alanine aminotransferase; ALP, Alkaline phosphatase; g/L, gram per litre; L/L, litre per litre; mmol/L, millimol per litre; μ mol/L, micromol per litre; g/L, gram per litre; U/L; Unit per litre

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The positive heartworm antigen test (Heska®) confirmed that the dog had heartworm disease although no microfilaria was detected on direct wet mount, Knott's concentration technique and Giemsa-stained thin blood films.

Lateral thoracic radiographs (Figure 1) showed alveolar patterns and increased opacity of the lung fields especially at the peri-hilar region which were suggestive of cardiogenic pulmonary oedema. On the dorsoventral view (Figure 2), the pulmonary trunk was severely enlarged and the pulmonary vessels appeared tortuous and enlarged, indicative of pulmonary hypertension. The loss of serosal details of abdominal radiographs (Figure 3) was suggestive of ascites.

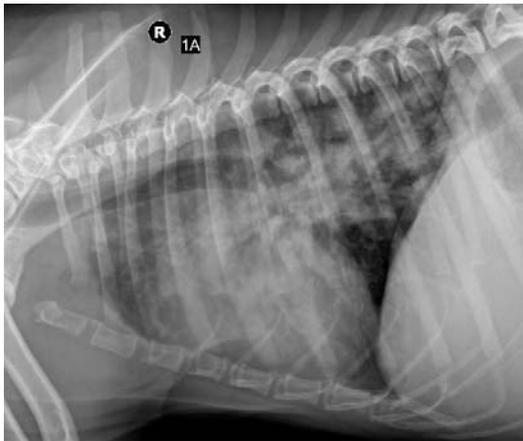


Figure 1. Lateral thoracic radiograph showed pulmonary oedema and enlarged pulmonary vessels.



Figure 2. Dorsoventral thoracic radiograph showed enlarged pulmonary artery and tortuous pulmonary vessels.



Figure 3. Dorsoventral abdominal radiograph showed a loss of serosal details due to ascites.

On echocardiography, the right ventricular chamber was dilated more than 3 times the size of left ventricular chamber (Figure 4). The interventricular septal wall was flattened and deviated towards the left ventricular chamber secondary to the elevated right ventricular pressure, as observed on both the right parasternal short and long axis views of the heart, which recorded an eccentricity index of 1.10 (Figure 5). The pulmonary artery was enlarged with pulmonic and tricuspid regurgitations. These findings confirmed a diagnosis of pulmonary hypertension. In addition, adult heartworms were detected within the pulmonary artery (Figure 6).

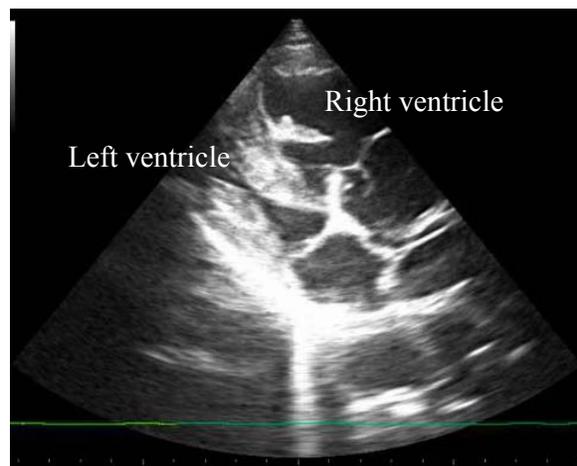


Figure 4. Echocardiographic image with right ventricular dilatation and flattening of the ventricular septum which deviated towards the left ventricular chamber secondary to the elevated right ventricular pressure.

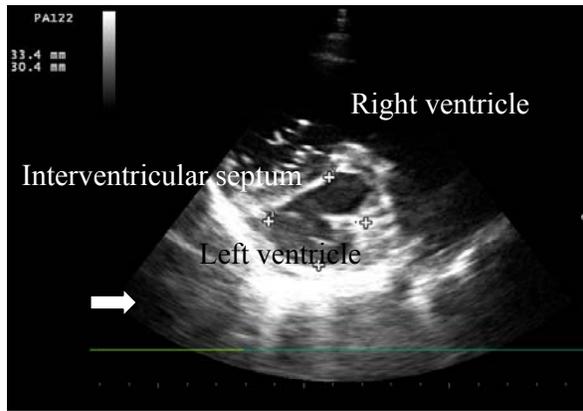


Figure 5. Echocardiographic image showed flattened interventricular septum and dilated right ventricle and eccentricity index of 1.10.

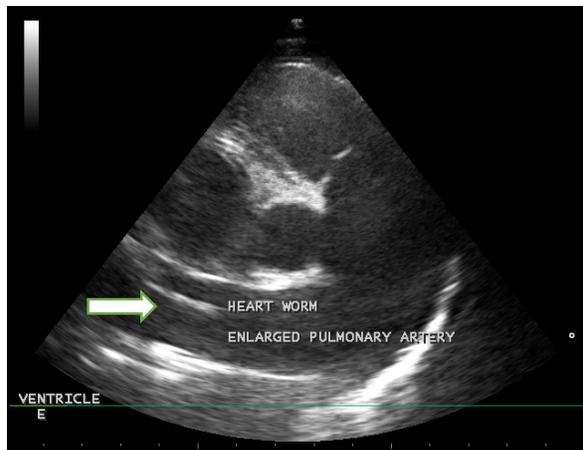


Figure 6. Echocardiographic image with dilated right ventricle and pulmonary artery. An adult *Dirofilaria immitis* appeared as a double parallel lines in the pulmonary artery as shown by the white arrow.

Based on the clinical signs, haematology and serum biochemistry results, radiographic and echocardiographic findings, the dog was diagnosed with severe heartworm disease with pulmonary hypertension and right-sided heart failure.

After a diagnosis was made, specific medical treatment was initiated which consisted of furosemide (2 mg/kg, IV; Frusemide, Troy Laboratories Pty. Ltd, Australia) for pulmonary oedema and ascites, tramadol hydrochloride (5 mg/kg, IV; Acugesic, CCM Duopharma Biotech, Malaysia) for coughing, benazepril hydrochloride (0.25 mg/kg, PO, SID; Fortekor, Novartis, Switzerland) for right-sided heart failure and sildenafil (1 mg/kg, PO, BID; Viagra, Pfizer, United States) for pulmonary hypertension. Abdominocentesis was carried out on the second and fourth day of hospitalisation and approximately 1.4 L and 0.8 L of serosanguinous fluid were removed respectively, to reduce the abdominal discomfort caused by ascites and for fluid analysis which revealed haemorrhagic effusion. A short course of antibiotics comprising of enrofloxacin (5 mg/kg, IV, SID; Baytril®, Bayer, Germany) and metronidazole (15 mg/kg,

IV, BID; Metrogyl®, Unique Pharmaceuticals, Texas) were administered for the presence of left shift neutrophilia, buccal petechiation and haematemesis which indicated a systemic infection. The protocol for the CHWD treatment was initiated, which consisted of ivermectin (Heartgard® Plus, Merial, Duluth), doxycycline (10 mg/kg, PO, SID) and prednisolone (1 mg/kg, SQ, SID) in accordance to American Heartworm Society (AHS) Guidelines 2014. Other supportive treatment included ornipural (2 mL, IV, BID; Vetoquinol, Mexico) as a hepatoprotectant, ranitidine (2 mg/kg, IV, TID; Rantac®, Unique Pharmaceuticals, United States) for antiemesis, and intravenous Lactated Ringer's for the 7% dehydration and the inappetence. On the fourth day of hospitalisation, melarsomine hydrochloride (2.5 mg/kg; Immiticide®, Merial, Duluth), was injected into the lumbar muscle as adulticidal therapy for the CHWD. The dog was under absolute cage rest throughout hospitalisation.

On the third day of hospitalisation, the pulmonary oedema reduced as assessed radiographically and clinically where the dog stopped coughing. The dog gradually regained its appetite and the abdominal distension reduced. On the eighth day of hospitalisation, the dog was discharged from the hospital for home management. The owner was instructed to provide cage rest, monitor the resting respiratory rate of the dog and complete the course of medication.

On the follow-up revisit two weeks later, the dog was bright and alert and the ascites had resolved. Overall, there was significant clinical improvement. Haematologically (Table 1), the red cell parameters increased, the thrombocyte count almost normalised while the leukocyte count decreased. The serum biochemistry analysis showed no remarkable finding except slightly elevated ALP probably due to the prednisolone administration as part of heartworm therapy since the hospitalisation. Pulmonic (Grade III/VI) and tricuspid (Grade IV/VI) murmurs but crackles lung sound persisted.

DISCUSSION

CHWD is caused by the filarial nematode *Dirofilaria immitis*, which resides in the pulmonary arteries, and occasionally the right heart chambers, of dogs, cats, ferrets and wild canids (McCall *et al.*, 2008). It is transmitted from the bite of an infected mosquito and their life cycle is completed in the heart of definitive hosts (Venco *et al.*, 2005). A study by Ng *et al.* (2012) reported a low prevalence (1.33%) of Dirofilariasis in Johor Bahru, Malaysia.

American Heartworm Society (2014) classifies CHWD based on clinical signs, that is, mild, moderate, severe, and caval syndrome. In this context, we diagnosed the dog with severe heartworm disease due to severity of the disease manifestations – dyspnoea, pulmonary oedema, ascites and congestive right-sided heart failure. Because clinical evolution of CHWD is usually chronic (Venco *et al.*, 2005), it was not surprising that the dog had non-responsive anaemia and monocytosis.

With reference to the American Heartworm Society (2014), the goals of treatment are to improve the dog's

clinical condition and to eliminate all life stages of the heartworms with minimal post-treatment complications. Dogs exhibiting significant clinical signs of heartworm disease should be stabilised prior to administration of adulticide treatment. In this case, the initial treatment for our patient was aimed at reducing the life-threatening congestive heart failure by a combined medical treatment (diuretic and angiotensin-converting enzyme inhibitor) and palliative therapy (oxygen supplementation and abdominocentesis). When the dog appeared brighter and less dyspnoeic on the fourth day of hospitalisation, the first adulticide injection of melarsomine hydrochloride was given. The following adulticide treatment was scheduled one month later (three-dose protocol). Meanwhile the dog was maintained on doxycycline for a complete course of 30 days, monthly heartworm prevention with ivermectin (Heartgard® plus) and prednisolone at a tapering dose, and provided with strict cage rest to prevent pulmonary thromboembolism.

In this case, the heartworm antigen test was positive but all the microfilarial tests inclusive of direct wet mount, Knott's concentration technique and Giemsa-stained thin blood film were negative for microfilariae. This coincided with the American Heartworm Society (2014) which stated that antigen testing is the most sensitive diagnostic method, whether screening a population of asymptomatic dogs or seeking verification of a suspected heartworm infection. AHS recommends that microfilaria testing to be done in tandem with antigen testing as antigen-antibody complexes may lead to false-negative antigen test results.

In CHWD, the development of pulmonary hypertension is reported at a prevalence of 6% (Pyle, 1995) and 9% (Johnson, 1993), respectively. The intimal proliferation of arteries occupied by living worms and/or embolic worm fragments from dead worms trigger thrombosis may completely obstruct segments of the pulmonary arteries resulting in an increase in pulmonary pressure (Carretón *et al*, 2012). This might explain the reason of the marked leucocytosis and thrombocytopenia as observed in this dog. Confirmed by thoracic radiography and echocardiography, this was the first case of CHWD with severe pulmonary hypertension presented in our veterinary hospital.

Although early treatment for CHWD yields a good prognosis, patients with advanced CHWD and severe clinical manifestations have a poor prognosis for survival. (Bowman and Atkins, 2009). Therefore, the prognosis for the dog was guarded due to the presence of right-sided heart failure and pulmonary hypertension. Although pulmonary hypertension is manageable by medication such as sildenafil, a selective phosphodiesterase inhibitor, it is unlikely reversible. In addition, dogs with pulmonary

hypertension generally have a median survival time of 3 to 91 days (Johnson *et. al.*, 1999).

CONCLUSION

Canine heartworm disease caused by *Dirofilaria immitis* can be classified into four classes in which the treatment depends on the classification. Prompt recognition and diagnosis of pulmonary hypertension in the event of heartworm disease is important to yield a prognosis and initiate specific treatment. As prevention is better than cure, year-round prophylaxis for heartworm disease is mandatory and should be encouraged.

ACKNOWLEDGEMENTS

The authors would like to thank all the staff of University Veterinary Hospital, Universiti Putra Malaysia.

CONFLICT OF INTEREST

No conflict of interest.

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