Canine Caval Syndrome

Clinicopathologic Conference

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INTRODUCTION

The canine heartworm, *Dirofilaria immitis,* is the most serious parasitic disease of the dog in North America, and is transmitted mostly by 10 to 15 species of mosquitoes.[2,3] The life cycle consists of five larval stages (L1 to L5) with L3 being the critical infective stage. After mating, the female worms release microfilariae (L1) into the host's bloodstream, where they can be ingested by feeding mosquitoes.[4] While in the mosquito, the larvae will molt twice (L1 to L2 to L3) and exit the proboscis during feeding to enter the canine bloodstream. Once the dog is infected, the L3 molts to L4 before traveling away from the inoculation site.[5] The final molt from the L4 stage to the L5 immature adult occurs 50 to 68 days after the initial infection. The 2-3 cm immature adults enter the vascular system and migrate to the heart and pulmonary arteries, where they mature into adult heartworms ranging from 20-30 cm over the next 99 to 152 days.[4,5] *Wolbachia pipientis* is an obligate symbiont bacteria that resides in the reproductive structures of *D. immitis* and is vital to the survival and reproduction of the parasite.[5]

Heartworm infections are divided into four categories of severity. Class 1 animals are asymptomatic or exhibit only mild clinical signs. Class 2 animals exhibit moderate clinical signs and radiographic abnormalities. Class 3 animals exhibit severe clinical signs and radiographic abnormalities consistent with right sided congestive heart failure.[3] Class 4 is also referred to as caval syndrome, vena cava embolism, vena cava syndrome, postcaval syndrome, acute hepatic syndrome, liver failure syndrome, or dirofilarial hemoglobinuria.[3,7] Caval syndrome is a serious life-threatening complication of chronic heartworm disease in dogs and cats.[7] It is associated with the movement of large numbers of heartworms from the diseased pulmonary arteries to the right ventricle, right atrium, and the caudal vena cava that causes obstruction of blood into and

through the right heart.[3,7] Without quick recognition, stabilization, and surgical intervention, caval syndrome can result in death in only a matter of hours.[3]

HISTORY AND PHYSICAL EXAM

Heartworm infection is most common in tropical and subtropical climates, but has been observed throughout most areas of the United States. Infection is inevitable in chronically unprotected dogs along the southern Atlantic, Gulf coasts, and other highly endemic regions. Dogs housed outdoors have a four to five fold increased risk compared to those housed indoors.[3] Caval syndrome occurs in 16% to 20% of dogs with heartworm disease, and is seen in most commonly in middle-aged male dogs in the spring and early summer.[7] Dogs presenting in caval syndrome typically have worm burdens greater than 60 (mean of 101), however numbers as low as 12 have been reported.[1,7]

Common owner observations of dogs with caval syndrome include an acute onset of inappetance or anorexia, lethargy, weakness, respiratory distress and, usually, dark, red-colored urine.[7] Coughing is less commonly reported by the owners, and many reports have no history of any known heartworm disease prior to the onset of signs.[4] Physical examination reveals signs of low cardiac output such as pale mucous membranes, tachypnea, tachycardia, and signs of right-sided heart failure such as jugular distention, jugular pulsations, engorgement of peripheral veins, and hepatosplenomegaly. Abdominal distention can sometimes be observed if ascites or hepatosplenomegaly are present, and on occasions mild jaundice can be detected.[7] Thoracic auscultation can often reveal a murmur of tricuspid insufficiency, splitting of the second heart sound, and cardiac gallop rhythms, in addition to increased bronchovesicular lung sounds.[2]

PATHOPHYSIOLOGY

The primary damage in heartworm infection occurs in the pulmonary arteries and lungs. The degree of damage is dependent on the number of worms present, the duration of infection, and the host's reaction to their presence.[1] The immature worms initiate vascular damage and lung pathology by causing eosinophilia and immune-mediated destruction that leads to signs of respiratory disease. The adult worms (L5) cause damage with the release of toxic substances that cause the host to have an immunologic reaction. Adult worms are also able to cause physical trauma due to their size.[4]

In caval syndrome, there is a sudden redistribution of worms to the right ventricle, right atrium, or the caudal vena cava, and it is not a direct reflection of the severity of pulmonary arterial disease.[3] The exact pathogenesis is not fully understood, but several theories have been proposed for the redistribution. Potential proposed causes include a high worm burden, simultaneous migration and arrival at the heart, delayed migration of maturing heartworms with simultaneous arrival at the heart, retrograde migration of adult heartworms in response to hemodynamic changes such as worsening pulmonary hypertension and reduced cardiac output, and migration due to administration of heartworm preventative or adulticide.[7] The redistribution of the heartworms causes blockage of blood flow through the right heart which leads to hemolysis and hepatic failure due to acute passive congestion.[3] Cardiopulmonary dysfunction occurs as a result of disruption of the tricuspid valve when the worm mass flows across it. This coupled with pulmonary hypertension exacerbates the tricuspid regurgitation, leading to volume overload of the right ventricle and reduced cardiac output.[7]

Hemoglobinuria thought to be a result of the red blood cells being destroyed as they pass through the worm mass.[4] The high rate at which the red blood cells are being destroyed exceeds

the liver's capacity to convert hemoglobin to bilirubin and results in the observed darker/red tinged urine. The anemia associated with this destruction leads to poor perfusion that leads to hepatorenal dysfunction.[7] Studies have showed that after the removal of the worms, plasma hemoglobin concentrations are drastically improved, and are typically normal within 24 hours.[7]

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for caval syndrome include those related to coughing, dyspnea, exercise intolerance, and syncope. These include but are not limited to congenital heart diseases, laryngeal paralysis, tracheal collapse, chronic bronchitis, upper or lower airway diseases, and pulmonary edema. Other considerations for the right-sided murmur include tricuspid valve insufficiency and degenerative valve disease. Causes of DIC such as septicemia, severe liver disease, and heat stroke should be considered for causes of hemoglobinuria.

DIAGNOSTIC APPROACH

Even though the presence of hemoglobinuria along with other discussed clinical signs has been considered pathognomonic for caval syndrome, echocardiography is the most important diagnostic test.[4,7] With this, the heartworm mass is able to be visualized moving across the tricuspid valve during diastole. In addition, right ventricular dilation and hypertrophy, abnormal septal movement, diminished left atrial and ventricle dimensions, and pulmonic and tricuspid insufficiency can also be visualized.[7]

TREATMENT: INITIAL STABILIZATION

Due to caval syndrome having an effect on so many organ systems, many patients present in a very unstable condition. A thorough physical exam, complete blood count, chemistry profile, urinalysis, echocardiography, electrocardiography, coagulation profile, blood gas analysis, and

blood pressure should be obtained prior to surgical intervention. Surgical intervention should be performed as soon as possible and should not be delayed solely for acquisition of the lab data. Supplemental oxygen should be started immediately to aid with the hypoxia-induced vasoconstriction, and fluid therapy should be initiated to aid in metabolic acidosis and decreased cardiac output. Caution should be used starting fluid therapy in dogs with an elevated central venous pressure. A catheter can be placed in the left external jugular vein for intravenous access and monitoring of central venous pressure, and blood products can be beneficial in severe cases.[7]

TREATMENT: SURGICAL INTERVENTION

Surgical intervention is indicated by the presence of hemoglobinuria, low output heart failure, anemia, and presence of heartworms within the tricuspid valve region on echocardiography. Heartworm removal can be done under light sedation or general anesthesia. The patient is placed in left lateral recumbency so that the right jugular vein is facing upwards.[7] The right cervical area is clipped and sterilely prepared.[6] Local infiltration of 2% lidocaine can be used prior to making an incision.[7] An incision is made over the right jugular vein, and the subcutaneous tissue is bluntly dissected to expose the vein.[6] Umbilical tape is placed proximally and distally to control hemorrhage.[7] An incision is made into the vein and a retrieval device, such as alligator forceps, is passed down the vein into the right atrium. Worms are gently extracted with multiple passes with 1 to 5 typically being removed at a time.[6] Multiple passes should be made until no more worms are retrieved on 3 to 5 consecutive attempts. The jugular vein is then sutured or tied off above and below the incision, and the skin is closed as normal.[6,7]

Another approach is often performed using fluoroscopic guidance and a basket device. The patient is prepared as previously described. A venotomy is performed on the vein and a wire guide is inserted into the vein into the right atrium, right ventricle, and pulmonary artery. The

wire guide is removed, and a basket device is inserted into an introducer and "spread-folded" to catch heartworms with the assistance of fluoroscopy. Passes are made until there are no more worms visible on echocardiography.[8] The vein and skin are then closed as previously described.

EXPECTED OUTCOME, COMPLICATIONS AND PROGNOSIS

Caval syndrome is resolved when the hemoglobinuria is resolved, there is a reduction or resolution in the tricuspid valve murmur, and central venous pressure has decreased with an increase in cardiac output.[7] Caval syndrome in dogs is associated with high mortality rates (30% to 40%) and generally has a guarded to poor prognosis even with removal of the heartworms.[1,7] It has been reported that high serum ALT activity has been associated with a decreased survival rate. Additionally, if a dog has high serum ALT and heartworms in the pulmonary artery on examination, the mortality rate is predicted to approach 100%. Disseminated intravascular coagulation and multi-organ failure have been reported as the primary cause of death before and after heartworm extraction.[1] In patients surviving the procedure, it is recommended they undergo staged heartworm treatment according to current American Heartworm Society standards, commencing approximately two weeks after surgery.[6,7]

CONCLUSION

Dirofilaria immitis is one of the most important parasites seen in dogs in North America. Caval syndrome is a rare but serious complication of *D. immitis* infections that can be fatal within hours unless the worms are surgically removed.[3] The diagnosis can be made quickly on physical exam and echocardiography, but even with surgical removal, the prognosis is grave.

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