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Heartworm Pathophysiology In Dogs And Cats

La Fisiopatologia de la Dirofilariosis en los Perros y los Gatos

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The severity of cardiopulmonary pathology in dogs and cats is determined by worm numbers, host immune response, duration of infection, and host activity level. *Dirofilaria immitis* the cause of heartworm disease in dogs and cats harbours an endosymbiont intracellular bacteria of the genus *Wolbachia* (a Rickettsia). Studies performed recently indicate that these bacteria may play an important role in the pathogenesis and immune response to filarial infection (Bandi et al, 2001).

In adult *D. immitis*, *Wolbachia* is present in the hypodermal cells of the lateral chords. In female worms, *Wolbachia* is also present in the ovaries and in developing embryos, but it is not present in the male reproductive apparatus (Sacchi et al. 2002). Experimental evidence indicates that infected hosts come into contact with *Wolbachia* and the *Wolbachia* Surface Protein (WSP) following the death of the parasite (by natural attrition, microfilarial turnover or pharmacological intervention).

**Pathophysiology in dogs.** A few days after arrival into the arterial system the young parasite causes mechanical damage to the walls of the pulmonary arteries. Endothelial cells are separated and appear inflamed, there is accumulation of WBC’s and the intima thickens. The endothelium grows villous like structures made of smooth muscle and intima. Heartworms cause the lining of the heart and pulmonary arteries to become rough and disrupt the flow of blood. This growth is stimulated by a Platelet Derived Growth Factor. The endothelial damage and the inflammatory reaction produce perivascular edema. Active dogs develop more pathology than inactive dogs for any given worm burden. Frequent exertion increases pulmonary arterial pathology and can precipitate clinical signs, including congestive heart failure. There is an increase of the peripheral resistance of the pulmonary arteries. The arteries become hard and can not expand when more oxygen is needed in exercise resulting in hypertension. Peripheral resistance can also be caused by a vasoconstriction which can be due to the inflammatory reaction, or to attempts to compensate local hypoxia, reduction of modulation of the smooth muscle tone caused by parasite or endosymbiont metabolites. Anatomical obstruction of the vessels by reduction of the arterial lumen due to the villous proliferations, emboli caused by live or dead parasites or in rare cases even microfilariae, secondary thrombi due to endothelial damage and parasite tissue. Pulmonary hypertension initially induces a dilation of the right ventricle with a compensatory hypertrophy of the myocardium. Congestive heart failure in severe cases induces ascitis, hydrothorax and hydropencardium. Presence of the parasite inside the heart could trigger mechanical valvular damage and endocarditis.

Pulmonary pathology is also exacerbated by natural or drug-induced worm death. High worm burdens are most often the result of inoculation from many mosquitoes over one season. Very large exposure can result in the vena cava syndrome the following year, typically in young dogs.

Heartworm-associated inflammatory mediators that induce immune responses in the lungs and kidneys cause vasoconstriction and possibly brochoconstriction. Leakage of plasma and inflammatory mediators from small vessels and capillaries causes parenchymal lung inflammation and edema. Pulmonary arterial constriction, especially with exertion, results in shear stresses further damaging the arterial endothelium.
Recently Kramer et al (2005) have shown that the predominance of IgG2 antibodies in heartworm infected dogs is indicative of a Th1-type, cell-mediated response. This may suggest that *Wolbachia* is involved in immune polarization during infection as well as exerting an inflammatory/immunomodulatory activity. Bazzocchi et al (2003) have recently studied the effect of *Wolbachia* Surface Protein from *D. immitis* on canine neutrophils and the results suggest that WSP stimulate neutrophil chemokinesis and IL-8 production. In dogs infected by *D. immitis* neutrophils accumulate in kidneys and in the walls of pulmonary arteries suggesting that *Wolbachia* could contribute to these inflammatory phenomena through its surface protein WSP.

**Pathophysiology in cats.** The disease in cats is different and more severe than that in dogs. The cat pulmonary arterial system is small and fine and the lungs respond violently to arriving larvae and adult heartworms.

Pulmonary enlargement has been described to occur rapidly indicating an intense host reaction. An exacerbated eosinophilic response of the smooth muscles and intima is frequently described. Pulmonary vascular narrowing and tortuosity frequently develops. Thrombosis in the pulmonary arterial branches may be caused by blood clots and worms or pieces of them that obstruct the narrow lumen of the arterioles. Embolization may be fatal even if caused by one worm.

Hydro or chylothorax is seen associated with chronic heartworm infections in cats usually associated with cor pulmonale and right heart failure. Pneumonitis may also develop as the lung parenchyma is infiltrated by eosinophils. Pulmonary edema caused by plasma from the pulmonary arteries associated to the proliferation and hypertrophy of type II cells potentially alter oxygen diffusion. Recently reported data (Dillon 2004) also indicates a marked decrease in activity of pulmonary intravascular macrophages in cats transplanted with dead or live adult heartworms.

As worms die, an intense pneumonitis develops; even one dead worm can produce severe pneumonitis, thromboembolism, and death. Pulmonary failure is possibly associated with pulmonary embolism. Recent data generated in dogs also suggests a potential immune-mediated reaction to *D. immitis* or perhaps *Wolbachia* surface protein antigens in the lungs that may cause an anaphylactic reaction.

**Recommended Reading**


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