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Angiostrongylus vasorum, pathophysiological aspects

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Overview

Angiostrongylus (A.) vasorum is a ubiquitous metastrongylid heart worm of dogs and related canids. It has an indirect life cycle with gastropods (slugs and snails) acting as intermediate hosts. The up to 25 mm long adult worms reside in pulmonary arteries and the right ventricle. After a prepatent period of around 40-60 days eggs are shed in terminal pulmonary arteries. Around at the same time as the infection becomes patent, intense immunological reactions against eggs and larvae cause severe inflammation in pulmonary vessels and parenchyma, including eosinophilic inflammation, hemorrhage, arterial thrombosis, periarteritis and coalescing granulomata. These pathological changes result in various degrees of radiographic changes. In experimentally-infected dogs, these abnormalities have been described to be most pronounced at 7-9 weeks post inoculation (wpi).

As may be expected based on the pathogenesis, cough and dyspnea are the most common clinical abnormalities, however, in some dogs respiratory signs may be completely absent but signs of various other organ systems dominate. These may include central nervous system signs, ophthalmological problems, immune-mediated thrombocytopenia or disseminated intravascular coagulation.

Pulmonary vascular inflammation and pulmonary thrombosis (PT) like in *Dirofilaria (D.) immitis* infection are important mechanisms of secondary pulmonary hypertertension (PH).

Pulmonary thrombosis and / or embolism (PTE)

As an entity, PTE in dogs is an important complication of a multitude of diseases, but its occurrence is probably underdiagnosed. Its presence may be suspected in patients with documented hypoxemia or hypercarbia, affected with a disease with known risk for PTE, coagulation abnormalities, suspicious radiographic findings, or the echocardiographic recognition of pulmonary hypertension (PH). Depending on the severity of PTE, however, arterial oxygen content, routine coagulation parameters (PT, PTT, TT), thoracic radiographs and echocardiography may be unremarkable. As outlined above, *A. vasorum* infection in experimentally infected dogs consistently

causes severe pulmonary lesions with PTE at the time of patency, and in naturally infected dogs has been shown to sometimes cause severe PH. Experimental infection of *A. vasorum* allows to study the effects of PTE on various above mentioned parameters in a well defined system.

Findings in experimentally infected Beagles

In one study, 3 healthy Beagles were experimentally infected with 50 and 3 with 500 larvae. Clinical and fecal Baermann examinations were done daily. Thoracic radiographs, femoral arterial blood gas analyses and echocardiography were performed 8 and 13 weeks (w) post infection (pi), and 9 weeks post therapy (wpt). Invasive pulmonary artery pressure (PAP) measurements under sedation were obtained 8 wpi. Four dogs were treated with a parasiticide at 13 wpi. The prepatent period lasted 47-49 days, and around the same time (42-56 days pi) the first respiratory signs were observed. Radiographic abnormalities were marked at 8 wpi with obvious progression to 13 wpi; besides pulmonary parenchymal lesions, several dogs developed pleural effusion. The pulmonary lesions were paralleled by moderate hypoxemia with a median PO₂ of 73 and 74 mmHg at 8 and 13 wpi, respectively. No 2D, M-Mode or Doppler echocardiographic changes, and no relevant PH were discernible at any time. Median calculated RV-RA-gradients were 24 mmHg at time 0, and ranged between 19 and 24 mmHg at the different time points pi and pt. Invasive PAP measurements at 8 wpi revealed median sPAP and dPAP of 31 and 15 mmHg, respectively. Radiographic lung changes and blood gas abnormalities correlated with clinical signs, but not with echocardiographic findings. In four of 6 dogs that were treated, the radiographic abnormalities had mostly resolved at 9 wpt, leaving only a mild interstitial pattern. Upon necropsy in 2 untreated dogs (infected with 50 and 500 larvae) subjectively the lungs were similarly affected. Histological lesions included severe inflammation, hemorrhage and thrombosis. In the four treated dogs, there was still evidence of thrombosis at the time of necropsy, 9 wpt. The mentioned interstitial pattern on radiographs in these was due to fibrosis. In this study, marked pulmonary changes in *A. vasorum* infection were not associated with abnormalities in cardiac function using conventional routine echocardiography and did not cause measurable PH. It was concluded that relevant PH may only develop at the time of acute and more severe pulmonary thrombosis. It was further speculated that newer ultrasound techniques might

be more sensitive to detect changes in right ventricular function in face of marked pulmonary disease.

The same 6 dogs were also examined by computed tomography to characterize the pulmonary lesions more exactly than with routine radiographs. Contrast CT was expected to help identifying arterial thrombosis. A first CT was done 13 weeks post infection (wpi) in all, and a second 9 weeks after treatment (wpt) in 4 dogs. CareDose was used to choose mA automatically as low as possible. Scanning parameters were 120 kV and a pitch of 1.2. Rotation time was 1 second. The images were reconstructed in 1.5 mm slices. The post contrast scan was done 20 seconds after administration of Telebrix[®] 35 (2.5ml/s, 2 ml/kg BW). At 13 wpi, severe consolidations with airbronchograms, large nodules and extensive areas of ground glass opacifications were found in the periphery of all lung lobes. Bronchi and lymph nodes were normal. Mild pleural effusion was found in five dogs. Post contrast CT revealed abruptly stopping vessels. At 9 wpt the consolidations, large nodules, pleural effusion and vascular abnormalities had resolved. Mild interstitial opacifications, subpleural interstitial thickening, subpleural lines and interface signs could still be observed, independent of the severity of the infection. In the very periphery of the airways slight bronchial dilatation could now be identified. Expectedly, CT allowed a much better and more exact judgment of lesion distribution and severity. However, for detection of PTE the CT results were disappointing. For one thing, the image quality using CareDose was not considered optimal and post contrast CT does not fulfill the requirements for angio CT.

In a second study the focus was put on newer echocardiographic modalities, i.e. Tissue Doppler Imaging (TDI) and contrast echo. An additional goal was to document arterio-venous shunting during experimental infection and during therapy. It was further hypothesized that PH may develop right at the time of treatment, when many worms die. In this study, six healthy Beagles were infected with 200 L₃ larvae. TDI (pulsed wave, RV longitudinal myocardial velocity basal segment), contrast echo with agitated saline and pulmonary transit time with SonoVue^R, as well as invasive PAP measurement were performed pre infection (T₀), once 7 to 12 weeks post infection (T₁) and once during the first five days after parasiticide therapy (T₂).

Tei and Tei_{TDI} indexes did not change over time. In the TDI variables analysed there was a decrease in peak myocardial velocity in systole (S_{TDI}) and an increase in time to peak systolic contraction (T_{peak}) with a median S_{TDI} of 0.130 m/s (0.123-0.194), 0.128

m/s (0.087-0.173) and 0.117 m/s (0.083-0.152), and a median T_{peak} of 0.097 ms (0.074-0.149), 0.109 ms (0.102-0.196) and 0.149 ms (0.104-0.234) at T0, T1, and T2, respectively. The E/A_{TDI} ratio decreased from T0 1.13 (0.94-1.55) to T2 0.91 (0.54-1.38). At T0 all dogs showed negative, and at T1 and T2 5 of 6 dogs showed positive contrast studies for shunts. Median pulmonary transit time was 4 beats respectively 2.3 seconds at T0 and no change was observed at T1 and T2. Invasively measured PAP slightly increased over time with median sPAP of 24, 25 and 29 mmHg and dPAP of 10, 11 and 18 mmHg, respectively. Two dogs showed mild PH at T2 (sPAP 33 and 30, and dPAP 20 and 25 mmHg); both had $E/A_{\text{TDI}} < 1$.

In conclusion, in dogs with marked pulmonary vascular disease and mild increase in PAP, effects on RV function were detectable using TDI but not conventional echo. In face of severe pulmonary disease the majority of dogs developed intrapulmonary arterio-venous shunts in the absence of relevant PH. Parasitocidal therapy did cause an increase in PAP, but not to a clinically relevant degree.

For most clinicians, plasma D-dimers have become an important tool to rule-out or -in PTE. In the second study, we therefore measured plasma D-dimers using an immunoturbidimetric method (and PT, PTT, TT). None of the dogs showed relevant changes in PT, PTT or TT. The values for plasma D-dimers were 0.17 (0.12-0.35) $\mu\text{g/ml}$ at T0, 0.37 (0.26-1.21) $\mu\text{g/ml}$ at T1, and 0.50 (0.26-2.37) $\mu\text{g/ml}$ at T2. Determination of D-dimers by immunoturbidometry was neither very sensitive nor specific to detect PTE in these experimentally infected dogs.

It is interesting to note that some naturally infected dogs do develop severe PH, but none of our experimental dogs did. It may be argued that infectious load and associated severity of (radiographically visible) pulmonary (artery) changes are the primary determinant of PH. However, it does not seem to be that simple, because some naturally infected dogs with most severe radiographic changes do not either develop PH. Maybe repeated infections with high infective loads are necessary to reach a point of PH. Alternatively an individual variability in respect to severity of immunologic response to *A. vasorum* may be an important factor. Finally, there may be individual variation in the capacity to open arterio-venous shunts; dogs that cannot open shunts may be the ones that develop the most severe PH.

References

- Boag, AK; Lamb, CR; *et al.* Radiographic findings in 16 dogs infected with *Angiostrongylus vasorum*. *Veterinary Record* 2004; 154: 426-430.
- Denkler, M; Makara M; *et al.* Thoracic computed tomography findings in dogs experimentally infected with *Angiostrongylus vasorum*. *Veterinary Radiology and Ultrasound* 2011; 52: 289-294.
- Estèves, I; Tessier, D; *et al.* Reversible pulmonary hypertension in a dog presenting simultaneously with an atrial septal defect and angiostrongylosis. *Journal of Small Animal Practice* 2004; 45: 206-9.
- Kranjc, A; Schnyder, M; *et al.* Pulmonary artery thrombosis in experimental *Angiostrongylus vasorum* infection does not result in pulmonary hypertension and echocardiographic right ventricular changes. *Journal of Veterinary Internal Medicine* 2010; 24: 855-62.
- Schnyder, M; Fahrion, A; *et al.* Haematological, clinical and pathological findings in dogs experimentally infected with the heart and lung nematode *Angiostrongylus vasorum*. *Parasitology Research* 2010; 107: 1471-80.