

## Investigation of the coagulation system in canine idiopathic pulmonary fibrosis

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Canine idiopathic pulmonary fibrosis (CIPF) is a progressive interstitial lung disease mainly affecting old West Highland white terriers (WHWTs). CIPF shares several clinical and pathological features with human IPF. An imbalance between thrombosis and fibrinolysis has been demonstrated in human IPF patients favouring a local and systemic prothrombotic state which correlates with disease severity and outcome. The aim of the present study was to investigate the coagulation and fibrinolysis systems in CIPF. For this purpose, coagulation profile and thromboelastography data were collected and compared between WHWTs affected with CIPF and unaffected WHWTs (CTRL). Coagulation times (PT, aPTT), plasmatic concentrations of fibrinogen, D dimers, antithrombin III, Protein S and Protein C activities, anti-factor Xa activity (FXa), and activated Protein C ratio (APCR) were retrospectively measured using the STA Compact automated coagulation analyzer from previously stored (-80°C) plasma samples obtained from 20 CTRL and 14 CIPF WHWTs. Point-of-care rotational thromboelastometer (ROTEM) was employed to prospectively measure clotting-time,  $\alpha$ -angle, amplitude at 10/20/30 min, maximal clot firmness, lysis after 30/60 min, and maximum lysis on whole-citrated blood sampled from 15 CTRL and 9 CIPF WHWTs. Statistical analyses were performed with a commercially available software using Student-t test or Mann-Whitney test for continuous variables, and Fisher's exact test for categorical variables. Statistical significance was set at  $P \leq 0.05$ . Compared with CTRL, WHWTs affected with CIPF demonstrated a longer aPTT (mean  $\pm$  SD) ( $12.2 \pm 0.9$  sec vs.  $11.5 \pm 0.7$ ,  $P = 0.028$ ), whereas results obtained in both groups were all within reference ranges. A trend for an increased fibrinogen concentration ( $4.1 \pm 1.8$  g/L vs.  $3.1 \pm 1.1$ ,  $P = 0.067$ ) and for a decreased APCR (median, range) ( $25.6, 21.9 - 27.7$  vs.  $26.8, 23.8 - 64.4$ ) in WHWTs affected with CIPF was observed, while there was no significant difference between groups for the other factors assessed. FXa was found above the upper limit of the reference range in 3 WHWTs affected with CIPF, but in none of the controls ( $P = 0.075$ ). ROTEM results demonstrated no significant difference between groups for any of the parameters studied. Results of the present study provide no clear evidence for a hypercoagulable state in WHWTs affected with CIPF. High fibrinogen concentrations found in CIPF WHWTs tend to suggest a proinflammatory state which may be a risk factor for thrombosis, but this finding should be confirmed by further investigation in larger cohorts of dogs.