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ATTI DEL LXIX CONVEGNO SISVET

Perugia, 15-17 Giugno 2015

Università degli Studi di Perugia

Dipartimento di Medicina Veterinaria

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HAEMOSTATIC PROFILE IN CANINE MULTIPLE MYELOMA: A COHORT STUDY IN 210 DOGS

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Human patients with MM have short survival times associated with frequent complications such as thrombosis.1 Considering their life span, dogs with MM in comparison to humans, have a longer survival times. Hypercoagulable complications in canine MM are not known and prognostic factors linked to haemostasis have been not thoroughly investigated.2

Aim of the study: a) to describe the haemostatic profile in dogs with MM at presentation, b) to assess whether coagulation parameters have a prognostic value, and c) to detect a possible hypercoagulable state.

Haemostatic abnormalities in dogs with MM (Group 1, #70) were evaluated via search of the electronic data-base (P.O.A System Plus 9.0 ®) of the San Marco Veterinary Clinic, between 2002-2015. Dogs included in Group 1 met the criteria: bone marrow plasmacytosis (plasmacells $\geq$15%), osteolytic lesions, serum mono-biclonal gammopathy. All groups had a haemostatic panel taken at presentation. Two groups of dogs matched for age, breed, and sex were enrolled as case-control: healthy dogs (Group 2,#70) and dogs affected by various diseases (Group 3,#70). The analytes investigated were: Platelet count (PLT), activated Partial Thromboplastin Time (aPTT), Prothrombin Time (PT), Fibrinogen, Thrombin Time (TT), Fibrin-Fibrinogen Degradation Products (FPDs), D-Dimer and Antithrombin (AT). In addition, within the MM-dogs the haemostatic profile between bleeding (B-MM, #42) and non-bleeding (NB-MM, #28) dogs was evaluated. Statistical differences between groups was evaluated by Kruskal-Wallis test and post-test analysis were performed by Wilcoxon-Mann-Whitney. Risk to death within B-MM and NB-MM dogs was evaluated by Pearson's X2 test. ROC curves were used to identify the best analyte to predict death. The significance level for all statistical test was set at $p<0.05$.

aPTT, PT and TT were significantly increased in Group 1 compared to Groups 2 and 3. PLT count and AT concentrations were significantly decreased in Group 1 compared to Group 2 and 3. Fibrinogen concentration was significantly decreased in Group 1 compare to Group 3, while no difference was present between Group 1 and 2. No difference were present between Groups 1 versus Group 2 and 3 for FDPs and D-dimer. PLT count and AT concentration were significantly decreased in B-MM compared to NB-MM; aPTT and PT were significantly increased in B-MM compared to NB-MM; finally, no differences between B-MM and NB-MM were present for TT, FDPs, D-Dimer. B-MM dogs showed lower mortality rate in respect to NB-MM patient ($p<0.028$). AT resulted the best haemostatic analyte in predicting death in dogs affected with MM ($p<0.04$; AUC 64%; 95% CI 0.50-0.78).

Primary and secondary haemostasis are highly compromised in dogs affected by MM while tertiary haemostasis appears to be not altered, suggesting that a hypercoagulable state, opposite to humans, is unlikely in dogs with MM. Surprisingly, in dogs with MM bleeding seems to have a protective effect against death. The best haemostatic assay to predict the mortality in canine MM at 90 days after the diagnosis is the AT.

1) Coppola A, Tufano A, Di Capua M, et al. Bleeding and thrombosis in multiple myeloma and related plasma cell disorders. Semin Thromb Hemost, 2011;37, 929-945.

2) Matus RE, Leifer CE, MacEwen EG, et al. Prognostic factors for multiple myeloma in dog. J Am Vet Med Assoc, 1986;188, 11:1288-1292.