Evaluation of Premature Platelet Aging or Platelet Desialylation in Dogs With Immune Thrombocytopenia

Bao, Annie (School: Auburn High School)

Immune thrombocytopenia (ITP), a life-threatening disorder of humans and dogs, leads to spontaneous bleeding from antibody-mediated platelet destruction. Standard immunosuppressive therapies for ITP cause dangerous adverse effects. New research in people with ITP and murine models show that in some cases, autoantibodies trigger premature platelet desialylation and accelerated hepatic clearance. If desialylation contributes to platelet destruction in canine ITP, sialidase inhibition may offer a novel, safe treatment. We hypothesized that platelet desialylation increases in ITP dogs vs healthy controls (HCs). HCs and ITP dogs were enrolled in this prospective observational study. Platelet-rich plasma (PRP) was isolated from EDTA blood. Native PRP and neuraminidase C (NeuC) treated PRP (representing maximal platelet desialylation) were incubated with FITC-labeled Ricinus communis agglutinin (RCA-FITC), a lectin which identifies desialylated platelets, and anti-CD61-PE antibody, a platelet marker. RCA-FITC fluorescence was quantified by flow cytometry, and the RCA-FITC ratio of native to NeuC-treated PRP was calculated, representing native platelet percentage of maximal desialylation (%MaxDes). ITP dogs had a significantly higher %MaxDes vs HCs (median 79.9% MaxDes [range 20.7-99.4%] vs 32.8% MaxDes [13.0-72.5%], p<.0001). CD61 platelet labeling was also reduced in ITP dogs vs HCs (1.1% CD61+ [0.3-65.0%] vs 96.1% CD61+ [66.3-99.3%], p<.0001). Platelets in ITP dogs are circulating in a highly desialylated state, suggesting that platelet desialylation contributes to pathologic platelet clearance in canine ITP; sialidase inhibitors may be a novel treatment. Loss of CD61 labeling could serve as a novel diagnostic biomarker for ITP, which is currently a diagnosis of exclusion.

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