Studies on pathogenesis of acute thrombosis in Phenylhydrazine treated rat

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Phenylhydrazine (PHZ) is well known for its ability to induce hemolysis via auto-oxidation of erythrocyte; however, there are few report about relevance to thrombosis. In this study, we investigated a short-term administration of PHZ caused acute thrombosis in rat lung (fibrinous thrombus in the alveolar capillaries), and determined the pathogenesis of the pulmonary thrombosis.

We repeatedly administered PHZ for a short period to rats and evaluated the time course change in hematology, histopathology in light and electron microscopy and mRNA expression. As a result, accumulation of deformed erythrocyte in the alveolar capillaries was observed preceding thrombus formation. The blood hypercoagulability, imbalance between coagulatory and fibrinolytic function which inclined to pro-coagulant force in vascular endothelium and limited endothelial injury in the alveolar capillaries were indicated mainly during the thrombus formation. In addition, gene expression profiling showed that inflammation/immune response was significantly and continuously induced in the lungs of PHZ-treated rats from the early phase of treatment.

To summarize the findings of our studies and other relevant reports, we propose a putative mechanism for acute pulmonary thrombosis in PHZ-treated rats as follows. PHZ affected erythrocytes and might cause various types of disruption, including loss of deformability and morphological alteration, which are attributable to regional stasis, endothelial dysfunction and systemic hemostatic disruption (i.e. blood hypercoagulability). Inflammatory condition in the lung provoked from early phase might induce the endothelial dysfunction. Considering the impact and the onset of the events observed in our study, regional stasis could serve as a trigger, and subsequent endothelial dysfunction in the lungs and blood hypercoagulability would be important contributors to acute thrombosis in the lungs of PHZ-treated rats.