[P-S-278] ABSENCE OF ADAMTS13 ON A VWF DEFICIENT BACKGROUND IS NO LONGER PROTHROMBOTIC IN A MURINE MODEL OF ARTERIAL THROMBOSIS

A.K. Chauhan, M.T. Walsh, D.G. Motto, D. Ginsburg, D.D. Wagner. Department of Pathology, Harvard Medical School, CBR Institute for Biomedical Research, Boston; Department of Internal Medicine, University of Iowa, Iowa; Department of Internal Medicine, University of Michigan, Michigan, United States

Introduction: In circulation Ultra-Large von Willebrand factor (UL-VWF) is cleaved by ADAMTS13 into a series of smaller multimers. We have shown that ADAMTS13 deficiency in the mouse results in accelerated thrombosis in injured arterioles. We reasoned that if VWF is the only ADAMTS13 substrate relevant for this model, then VWF deficiency would result in the abrogation of the effect of ADAMTS13 deficiency. Alternatively, if we observe an effect of ADAMTS13 deficiency on thrombus formation in the absence of VWF, this would suggest the existence of an ADAMTS13 substrate (s) in addition to VWF.
Methods: We crossed Adamts13-/- mice on a VWF-/- genetic background. Using the ferric chloride injury model we compared experimental thrombosis in arterioles of Adamts13-/-/VWF-/- mice with VWF -/- mice by intravital microscopy.
Results: Since Adamts13-/- mice of mixed genetic background were used in early studies, we first confirmed our previous findings of accelerated thrombus formation, in Adamts13 -/- on C57BL6/J background. In the Adamts13-/- mice, thrombi >20 μm were seen at 5.7 ± 0.5 min as compared to 7.9 ± 0.4 min in wild-type (WT) mice ($P<0.005$). The vessels occluded in Adamts13 -/- mice in 10.8 ± 1.0 min after injury compared to 14.6 ± 1.3 min in WT mice ($P<0.05$). Then we compared experimental arterial thrombosis in VWF-/- and Adamts13-/-/VWF-/- mice. The thrombi grew slowly in the absence of VWF. But the mean time to form first thrombus > 20 μm in Adamts13-/-/VWF-/- (10.7 ± 0.4 min) was similar to VWF-/- mice (10.6 ± 0.7 min). The rate of individual thrombus growth in Adamts13-/-/VWF-/- was also similar to VWF-/- thrombi. After 40 min of observation, thrombi failed to grow to occlusive size in either the Adamts13-/-/VWF-/- or VWF-/- mice.
Conclusions: The absence of ADAMTS13 in the setting of VWF-deficiency is no longer prothrombotic in arterial thrombosis, suggesting that at least in this model system, VWF is the only ADAMTS13 substrate relevant to thrombus growth and stability at arterial shear.
Chauhan AK, Walsh MT, Motto DG, Ginsburg D, Wagner DD. ABSENCE OF ADAMTS13 ON A VWF DEFICIENT BACKGROUND IS NO LONGER PROTHROMBOTIC IN A MURINE MODEL OF ARTERIAL THROMBOSIS. *J Thromb Haemost 2007*; **5** Supplement 2: P-S-278

Date: Sunday, July 8, 2007
Session Info: Poster: TTP/HUS and ADAMTS 13
Room: Exhibition Area