종근당 신진연구비

급성신손상 동물모델에서 ADAMTS13의 역할 및 신보호효과 연구

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ADAMTS13–Von Willebrand Factor (vWF) Axis is Involved in the Pathophysiology of Renal Ischemia Reperfusion Injury

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Recent epidemiologic studies showed that impaired activity of ADAMTS13, a protease cleaving Von Willebrand factor (vWF) multimer, could predict renal complications in diabetic patients. The ADAMTS13- vWF axis was also suggested to play a critical role in the pathophysiology of ischemia-reperfusion injury (IRI) in different organs. The purpose of this study was to investigate whether ultralarge vWF (UlvWF)-multimer was involved in the development of AKI and a potential role of ADAMTS13 in renal IRI. We performed renal IRI in ADAMTS13 knockout (KO) mice or wild type (WT) mice. Functional, histological kidney damage, inflammation were compared and the effect of recombinant human ADAMTS13 (rhADAMTS13) in ADAMTS13 KO mice was also assessed. Following IRI, vWF was detected in both medulla and cortex of injured kidney by immunohistochemistry. Western blot analysis also showed increased expression of ULvWF-muiltimer in ischemic kidneys, and the expression was significantly higher in ADAMTS13 KO mice than WT mice. The higher level of vWF-multimer in ADAMTS13 KO mice was correlated with more functional deterioration and severe tubular injury, suggesting an important role of VWF in renal IRI. In addition, the number of Gr-1 (+) neutrophils were significantly higher in the kidney of ADAMTS13 KO mice compared to that of WT mice, whereas F4/80 macrophages were not. In ADAMTS13 KO mice, administration of rhADAMTS13 after IRI partially restored renal injury, suggesting that ADAMTS13 deficiency is a key player that exacerbates renal IRI associated with vWF. Our data shows that ADAMTS13-vWF axis is critically involved in the pathophysiology in renal IRI. This is first report showing the involvement of UlvWF-multimer in renal IRI indicating that ADAMTS13 could have therapeutic value to limit renal ischemia/reperfusion injury.

Key Words: 급성신손상, ADAMTS13, 폰빌레브란트 인자
Acute kidney injury, ADAMTS13, Von Willebrand factor