Renal tubular injury exacerbated by Vasohibin-1 deficiency in a murine cisplatin-induced acute kidney injury model

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Running head: Vasohibin-1 in cisplatin-induced AKI

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Abstract

Acute kidney injury (AKI) is frequently encountered in clinical practice, particularly secondary to cardiovascular surgery and administration of nephrotoxic agents, and is increasingly recognized for initiating a transition to chronic kidney disease. Clarifying the pathogenesis of AKI could facilitate the development of novel preventive strategies because the occurrence of hospital-acquired AKI is often anticipated. Vasohibin-1 (VASH1) was initially identified as an antiangiogenic factor derived from endothelial cells. VASH1 expression in endothelial cells has subsequently been reported to enhance cellular stress tolerance. Considering the importance of maintaining peritubular capillaries in preventing the progression of AKI, this study aimed to examine whether VASH1 deletion is involved in the pathogenesis of cisplatin-induced AKI. For this, we injected male C57BL/6J wild-type (WT) and VASH1 heterozygous knockout (VASH1$^{+/-}$) mice with either 20 mg/kg of cisplatin or a vehicle solution intraperitoneally. Seventy-two hours after cisplatin injection, increased serum creatinine concentrations and renal tubular injury accompanied by apoptosis and oxidative stress were more prominent in the VASH1$^{+/-}$ mice than in the WT mice. Cisplatin-induced peritubular capillary loss was also accelerated by VASH1 deficiency. Moreover, the increased expression of intercellular adhesion molecule-1 in the peritubular capillaries of cisplatin-treated VASH1$^{+/-}$ mice was associated with a more marked infiltration of macrophages into the kidney. Taken together, VASH1 expression could have protective effects on cisplatin-induced AKI probably through maintaining the number and function of peritubular capillaries.

Keywords: Vasohibin-1, Acute kidney injury, Cisplatin, Peritubular capillary, Endothelial cells