Intensive Care Nephrology

Inflammasomes in Experimental Model of Acute Kidney Injury

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Early inflammation in acute kidney injury (AKI) is largely mediated by the innate immune system, which uses pattern-recognition receptors (TLRs, NLRs) to detect danger signals such as pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs). Within the cytoplasm, NLR protein (NLRP) forms a complex, the inflammasome with ASC and inactive caspase-1. Caspase-1 is activated in the inflammasome and acts as a mediator of both cisplatin-induced AKI (Cis-AKI) and ischemic AKI.

NLRP3 was present in macrophages in culture, but the lack of protection by macrophage depletion argues against the macrophage as a source of injurious NLRP3 inflammasome in Cis-AKI. NLRP3 were expressed in CD4 T cells and CD4 T cell depletion markedly protected against Cis-AKI. An increase in caspase-1, IL-1α and IL-1β in cisplatin-treated proximal tubules (Cis-PTs) that was not associated with an increase in NLRP3 and the lack of protection against Cis-AKI in NLRP3 -/- mice suggests that the activation of caspase-1, IL-1α and IL-1β may be independent of the NLRP3 in Cis-PTs. However, two previous studies have reported protection against ischemic AKI in NLRP3 -/- mice. NLRP3-deficiency protected mice against ischemic AKI associated with pro-inflammatory cytokines. In another study, NLRP3 caused AKI, on the contrary, by a direct effect on renal tubular epithelium, and was independent of pro-inflammatory cytokine activation

The difference in protection against Cis-AKI vs. ischemic AKI in NLRP3 -/- mice was not explained by differences in pro-inflammatory cytokines. Thus, the role of other inflammasomes merits further study in the experimental model of AKI.