

패혈증성 급성신손상 발생에서 신장세포 자멸사(apoptosis)의 역할

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Role of Renal Cell Apoptosis in Pathogenesis of Septic Acute Kidney Injury

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Introduction: The presence of acute kidney injury (AKI) in septic patients is known to be associated with worse outcome. However, mechanisms of septic acute kidney injury (AKI) remains elusive and several recent reports suggest that excess immune suppression characterized by massive lymphocytes apoptosis might be causally linked to sepsis mortality or sepsis induced organ dysfunction. In addition to immune cell apoptosis, renal cell apoptosis has also been demonstrated in animal models of sepsis or some autopsies. However, the exact role of renal cell apoptosis in the development of AKI in sepsis has never been assessed.

Method: To examine the role of renal cell apoptosis in septic AKI, we used cecal ligation and puncture (CLP) method in C57/BL6 mice with or without pretreatment with caspase 3 inhibitor. To further dissect out the role of renal cell apoptosis independent of immune cell apoptosis, we also performed CLP in mature T and B lymphocyte deficient RAG-1 deficient mice and examined the effect of caspase 3 inhibition on apoptosis as well as on renal function.

Results: In C57/BL6 mice, plasma creatinine increased on day 1 after CLP and despite lack of overt tubular necrosis, significantly increased numbers of renal cell apoptosis were observed. Kidney caspase 3 activity showed positive correlation with plasma creatinine and pretreatment with caspase 3 inhibitor markedly attenuated functional impairment. Similar with WT mice, CLP also evoked mixed gram negative and positive bacterial peritonitis induced sepsis with multiple organ dysfunction in RAG-1 deficient mice. Furthermore, in the absence of mature T and B lymphocytes, that are known to undergo apoptosis in sepsis, pretreatment with caspase 3 inhibitor still partially rescued RAG-1 deficient mice from development of AKI with significant reduction of plasma cytokines (IL-6, IL-10, TNF- α , MCP-1).

Conclusion: These results demonstrated the important role of renal cell apoptosis in the development of AKI and strategies that suppress renal cell apoptosis might be useful in preventing or treating AKI associated with sepsis.

Key Words: 패혈증, 급성신손상, 세포자멸사

Sepsis, Acute kidney injury, Apoptosis