Lunch Seminar 2

DATE
Wednesday, October 5, 2016 12:05-13:05

VENUE
Room 1 (Aurora)  Tokyo Dome Hotel, Tokyo, Japan

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Title
Role of Endotoxin in Septic AKI

Sponsor: The 8th Congress of the International Federation of Shock Societies
Toray Industries, Inc. / Toray Medical Co., Ltd.
Role of endotoxin in septic AKI

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Sepsis and acute kidney injury (AKI) are the most common severe complications for critically ill patients in ICUs. The prognosis of patients with both sepsis and AKI are extremely poor and their mortality rate is an unacceptably high. Of note, sepsis and AKI synergistically worsen the outcomes of ICU patients.

Endotoxin, a lipopolysaccharide derived from the outer membrane of gram-negative bacteria, is recognized as a key factor in the sepsis cascade because it triggers a series of inflammatory reactions that lead to organ dysfunction including AKI. It is widely known endotoxin can cause AKI by several different pathways such as alternating renal hemodynamics and direct tubular cell injury. Recently, a basic study demonstrated reduction of urine flow rate in the early phase of endotoxemia by using two-photon inravital microscopy. Decreased urine flow rate was dominantly observed around the renal tubules in which endotoxin accumulated via TLR4-dependent uptake. Another study reported the role of macrophage in endotoxin preconditioning. Endotoxin preconditioning is a preventative treatment against subsequent larger exposures to endotoxin. It is assumed that endotoxin preconditioning downregulates the inflammatory response of immune cells. Small amount of endotoxin injection caused clustering of M2 macrophages around S1 proximal tubules. Genetically engineered animal experiments demonstrated that CD14-expressing macrophages were necessary for tubular protection after preconditioning.

Endotoxin adsorption by direct hemoperfusion with polymyxin B-immobilized fiber column (PMX-DHP) has been widely used for sepsis. Although several promising results have been reported so far, currently available evidence does not strongly support PMX-DHP against sepsis. The Diagnostic Procedure Combination (DPC) database is a Japanese nationwide administrative claim database representing approximately half of all inpatient admissions to acute care hospitals. By using the DPC database, we conducted retrospective analysis with propensity score matching and demonstrated that not post-abdominal surgery septic shock but septic shock complicated with severe dialysis-requiring AKI might benefit from PMX.

In conclusion, endotoxin appears to play an important role in sepsis and septic AKI, however many different aspects of endotoxin need to be considered for application of endotoxin removal treatment in human sepsis.