KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Oral Communication Abstract
Presentation No. PL2-01 (Abstract Submission No. 2215)

Plenary Lecture 2 Sep. 3 (Fri), 14:00-15:00

The brain-gut-kidney axis in the development of cognitive dysfunction following acute kidney injury (AKI)

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Objectives: Although epidemiological studies suggest that long-term survivors of dialysis requiring AKI show increased prevalence of dementia, its underlying mechanisms remain uncertain. Based on recent data showing kidney-gut crosstalk mediated by immune modulation in AKI, we hypothesized that gut dysbiosis and aberrant gut immune response might contribute to the cognitive dysfunction following AKI.

Methods: Thirty min ischemia/reperfusion injury (IRI) was performed in C57/BL6 mice. Cognitive dysfunction, histological damage including blood-brain barrier (BBB) disruption, inflammation, gut microbiome and immune cell activation were determined at 6 months after IRI.

Results: Glomerular filtration rate showed complete recovery of renal function at 6 months after IRI. However, in the open field behavior test, IRI mice traveled shorter distance and walked more slowly compared to sham, suggesting the development of cognitive dysfunction long after kidney IRI. Evans blue dye extravasation showed disrupted BBB and the number of microglial cells, amyloid-beta deposits increased in the brain in IRI mice. Principal coordinate analysis of gut microbiome in IRI was clearly distinguished from that ofsham. Despite no difference in alpha-diversityRelative increase of abundance of bacterial families of Saccahrimonas, Erysipelotrichaceae, Bacteroidaceae, Lactobacillaceae while decrease of Lachnospiraceae and Prevotellaceae were the hallmark of dysbiosis. Flow cytometry of gut immune cells showed a significantly increased percentage of IL-17A+CD4+ cells in small intestine, whereas percent CD25+CD4+ Tregs decreased significantly in colon, showing the gut immunity moving toward inflammation long after AKI.

Conclusions: This is the first animal study that showed the development of structural brain injury and cognitive dysfunction long after AKI. Given that the important role of dysbiosis in various neurologic diseases, presence of dysbiosis and gut inflammation at 6months after IRI might contribute to the development of long-term neurologic sequelae of AKI. Targeting the gut might be a novel therapeutic target for prevention of long-term adverse outcomes in AKI patients.