OS01-1 Pathogenesis of progression of influenza virus infection, muti-organ failure and encephalopathy

◯Hiroshi KIDO[1], Junji CHIDA[1], Kazuhiko YAMANE[1], Min YAO[1]
[1]Inst. for Enzyme Research, The Univ. of Tokushima

Aims: Severe influenza causes significant morbidity and mortality. Pathogenesis of severe influenza in high risk patients is mainly derived from metabolic disorder of patients. Here we analyzed the metabolic disorder of severe influenza patients.

Results and Discussion: Severe influenza is characterized by cytokine storm and multiorgan failure on vascular hyperpermeability. Influenza A virus infection resulted in significant increase in TNF-α, IL-6, IL-1β, viral hemagglutinin processing protease trypsin and matrix metalloprotease-9. These upregulated factors are closely related and enhance to each other in the influenza-cytokine-protease cycle. Upregulated ectopic trypsin by viral infection and cytokine upregulation mediates the post-translational proteolytic cleavasge of viral envelope hemagglutinin, which is crucial for viral entry and replication and subsequent tissue damage in various organs. Trypsin induced intracellular calcium mobilization through PAR-2 receptor and loss of tight junction constituent, zonula occludens-1, resulting in endothelial hyperpermeability. Many of the high risk patients have lipid metabolic disorder, because fatty acid oxidation could ensure as much as 70% of the ATP generation in endothelial cells. The metabolic disorder enhances the pathogenesis of influenza-cytokine-protease cycle.