Jingchun Song, J Bacteriol Parasitol 2013, 4:4
http://dx.doi.org/10.4172/2155-9597.S1.004

OMICS Group Conferences
Accelerating Scientific Discovery

International Congress on
Bacteriology & Infectious Diseases
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, MD, USA

TIMP-1/TIMP-2 ratio, a novel biomarker for early prediction of sepsis-induced disseminated intravascular coagulation

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Severe sepsis remains a serious problem worldwide, with intensive care unit death rates ranging between 30% and 70% even under the best of care. Sepsis generally results from the release of cytokines and the activation of plasma protein cascades such as the coagulation and fibrinolytic systems. Disseminated intravascular coagulation (DIC) is a complex syndrome characterized by activation of the haemostatic and fibrinolytic systems with increasing loss of localization and compensated control. DIC is a common complication of sepsis and is associated with a poor outcome. Within this process, activation of coagulation, inhibition of fibrinolysis and consumption of coagulation inhibitors lead to a procoagulant state resulting in inadequate fibrin removal and fibrin deposition in the microvasculature. Eventually, diffuse obstruction of the microvascular bed gives rise to progressive organ dysfunction, such as renal insufficiency, acute respiratory distress syndrome, hypotension and circulatory failure. Because of consumption of coagulation factors and the interference of fibrin degradation products, diffuse bleeding may occur.

Early warning signs of DIC are often nonspecific and subtle, but the clinical course may be alarmingly fulminant, leading to death within days of onset. Thus, early identification of sepsis-induced DIC is a major diagnostic problem. In 2001, an International Society of Thrombosis and Haemostasis (ISTH) subcommittee divided DIC into two stages: non-overt DIC with a stressed but compensated haemostatic system; and overt DIC with a stressed and uncompensated haemostatic system. On this basis, a scoring system for overt DIC was proposed by the ISTH, using which overt DIC can be diagnosed in 25% in patients with sepsis. However, these diagnostic algorithms remain far from gold standard.

Much basic and clinical research has been focused on the crossroads of coagulation and inflammatory pathways that is important in the pathogenesis of sepsis and DIC. As key factors in coagulation and immune mediators, platelets not only "plug the leak" in a damaged vessel, but also secrete chemokines and proinflammatory cytokines essential for host defense against microbial infection. Regarding the pathogenesis of sepsis-induced DIC, these platelet-derived factors warrant research into their use for early diagnosis and prediction of outcome. To identify valuable diagnostic biomarkers of sepsis-induced DIC among various platelet-derived factors, a protein microarray kit was customized for use with a mouse cecal ligation and puncture (CLP) model. Platelet-derived factors were detected by protein microarray analysis at different times up to 72 h in the CLP model. Tissue inhibitors of metalloproteinase TIMPs as biomarker chosen from platelet-derived factors were valued in severe sepsis patients with DIC.

Biography

Song Jingchun has completed his M.D. at the age of 35 years from the Second Military University. He is the director of ICU in Changcheng Hospital affiliated to Nanchang University.

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