Letter

DIC in COVID-19: Implications for Prognosis and Treatment?

The ongoing COVID-19 pandemic is an exceptional challenge for the health systems throughout the world. So far, no causative therapy nor protective vaccines are available. In several countries, the capacities for intensive care and for support in case of acute respiratory distress syndrome (ARDS) are overstretched, and the mortality is considerable. In this situation, useful prognostic parameters and targeted supportive treatment are urgently needed.

Recently, Tang et al.[1] reported about the frequent occurrence of DIC in COVID-19 patients with serious respiratory failure. DIC, as diagnosed according to the validated ISTH criteria[2], was much more frequent in non-survivors (71.4 %) than in survivors (0.6%). This suggests that establishing the diagnosis of DIC by the validated and recognized ISTH tool[2] might be useful as readily assessable prognostic parameter, warranting enhanced vigilance[3] and further research into pathophysiology and clinical impact of DIC in severe COVID-19..

Moreover, it appears reasonable to formulate the hypothesis that DIC might not only be a concomitant finding, but even a pathophysiological process contributing to circulatory and organ failure, in COVID-19 particularly pulmonary damage. As well know from DIC e.g. in bacterial sepsis, disseminated fibrin deposits occur in the microvasculature, impairing the perfusion and thus performance of vital organs. In this context, it is of interest that in three patients with severe COVID-19 pneumonia induced ARDS Tissue Plasminogen Activator (tPA) treatment resulted in documented but transient improvement of pulmonary function parameters[4]. This would be compatible with the assumption that during tPA infusion the pulmonary microvasculature was partially reopened, but after terminating tPA the microthrombi inceased again, due to the ongoing inflammatory stimulus perpetuating DIC.

If the above hypothesis would be correct, it might be warranted to think about possible interventions to attenuate DIC and prevent further obstruction of organ microvasculature by fibrin deposits. The key player in the generation of fibrin deposits is thrombin. Thus, for decades several approaches of anticoagulation have been evaluated for beneficial effects in DIC, particularly in sepsis. These trials have been admittedly so far frustrating. For none of the approaches could a clear and proven survival benefit be demonstrated, as shown in a recent meta-analysis[5]. However, some of the clinical studies conducted so far had considerable flaws. For instance, the large randomized multicenter KyberSept trial[6] used exceedingly high Antithrombin III (AT) doses, in many patients accompanied by effective heparin doses, resulting in excessive bleeding. In their meta-analysis[5], Umemura et al. showed that AT nevertheless did show a small reduction of mortality (risk ratio 0.63; 95% CI 0.45; 0.90) in the subgroup of sepsis patients with DIC. Also a recent summary[7] of systematic reviews found some evidence, albeit with low certainty for a beneficial effect in sepsis-induced DIC, and mentioned that the Japanese Clinical Practice Guidelines for Management of Sepsis and Septic shock weakly recommended the use of antithrombin for DIC patients with reduced antithrombin activities.

Thus, it might be time for reconsidering the interaction and modulating of different connected systems e.g. coagulation, fibrinolysis, Kallikrein-Kinin, Complement and immunity (cytokine storm). A rationale for developing strategies for attenuating DIC in COVID-19. If such efforts would be successful, it might have immense benefit also for intensive care patients far beyond the current crisis.

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Rainer Seitz, M.D.
retired from Paul-Ehrlich-Institut
Langen, Germany. E-Mail: Rainer-Seitz@t-online.de

Wolfgang Schramm, M.D.
emeritus Ludwig-Maximilians Universiy
(LMU) Rudolf Marx Stiftung
Munich, Germany. E-Mail: Wolfgang.Schramm@med.uni-muenchen.de

Rainer Seitz wrote the manuscript; both authors contributed to the concept, literature search and conclusions.

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