

Letter to the Editor

The complement inhibitors in COVID-19: future expectations

Dear Editor,

Diurno et al¹ reported four patients with coronavirus disease 2019 (COVID-19) related acute respiratory distress syndrome successfully treated with eculizumab, a complement C5 inhibitor. These findings suggest a role of complement activation in the virus-induced lung damage that was previously shown in animal models². Moreover, recent studies revealed deposits of complement components in lung biopsy samples and elevated serum levels of C5A in patients with severe COVID-19^{3,4}. However, it is still unknown which COVID-19 patients will develop a pronounced complement activation and may benefit from complement inhibitors, and whether it is possible to predict efficacy of treatment.

It seems that in predisposed patients, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) may induce an uncontrolled complement activation, an analogue to cytokine release syndrome, or cytokine storm, leading to the development of complement-mediated thrombotic microangiopathy (TMA) in the lung and other organs. A predisposition to TMA may be determined by both non-specific factors, including the severity of the immuno-inflammatory and/or prothrombotic response, and genetic factors, such as mutations in the complement system genes.

We suggest that generalized TMA, particularly in combination with multiple organ failure and signs of complement activation (abnormal changes in complement protein levels and activity), may be an indication for complement inhibition in COVID-19 patients. Such patients will probably require short course of treatment, since "complement storm" results from transient hyperinflammation and/or hypercoagulability. In fact, Diurno et al¹ have achieved a positive clinical effect after 2 infusions of eculizumab. Importantly, a shorter course of treatment will reduce the risk of secondary infections and the cost of therapy.

In summary, Diurno et al¹ showed that complement inhibitors may be beneficial for patients with severe COVID-19, given a crucial role of complement in the genesis of SARS-CoV2-infection. However, the specific indications for treatment with eculizumab need to be clarified.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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