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CE - LETTER TO THE EDITOR

COVID-19, coagulopathy and venous thromboembolism: more questions than answers—comment

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Dear Editor,

We found very interesting the recent paper by Marietta et al. [1] on coagulopathy in coronavirus disease 2019 (COVID-19) patients. They stressed that abnormal coagulation parameters in patients with COVID-19 were associated with a poor prognosis, and that the incomplete comprehension of coagulation disorder pathogenesis is hampering therapeutic approaches. Hence, they propose to investigate in greater depth the mechanisms underlying this disease. Several parameters were reported to associate with microthrombosis and poor prognosis in COVID-19 patients. Endothelial activation was noted as an important component by several authors, a fact leading to the release of von Willebrand Factor (vWF) that will interact with platelets; indeed, examination of platelet dynamics found a small but highly activated platelet subpopulation in severe cases. In addition, they compared the neutrophil activation state from severe COVID-19 cases, namely those requiring mechanical ventilation, and from patients with less severe disease who only required oxygen therapy, and observed that neutrophils were highly upregulated in severe cases. A list of factors involved in the coagulopathy encompasses elevated circulating levels of vWF and fibrinogen, and their interactions with endothelial cells and thrombocytes for the most severe cases of COVID-19. It was also reported that high levels of the cytokine proteins interleukin (IL)-6 and tumor necrosis factor (TNF)-α on admission to hospital with COVID-19 predicted a worse outcome with respect to that observed in patients with low levels. Hence, the proposal that serum IL-6 and TNF-α levels should be considered in the management and treatment of COVID-19 patients to stratify prospective clinical trials, guide resource allocation, and inform therapeutic options. Why only a fraction of patients succumbs to the severe disease? Possibly, a further factor is involved in precipitating microthrombosis in a subset of patients. One pathogen that activates endothelial cells and platelets, binds vWF to platelets, and greatly increases levels of IL-6 and TNF-α is widely recognized: the pathogenic strains of *Helicobacter pylori*, i.e. those that produce a vacuolating toxin and express the proinflammatory CagA protein [2–5]. We propose that the prudent physician should test for these strains in COVID-19 patients with coagulopathy and high IL-6 levels. It cannot be excluded, in fact, that cases with unfavorable outcome are those in which high systemic concentrations of proinflammatory cytokines due to the underlying *H. pylori* infection further increase due to the supervened SARS-CoV-2 infection.

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