CORRESPONDENCE

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MicroCLOTS pathophysiology in coronavirus disease 2019

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The multifaceted clinical manifestations of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are likely to be explained by a complex pathophysiology which has not been completely elucidated.

It is known that SARS-CoV-2 infects the host cells through the cell surface receptor of angiotensin-converting enzyme 2 (ACE2); this receptor is expressed in multiple organs, and particularly in the arterial and venous endothelial cells; hence, it's almost ubiquitous characteristic. It is also generally accepted that, in addition to the direct cellular damages caused by SARS-CoV-2, a key role in severe cases is played by an abnormal and disproportionated immune response from the host [1].

We have recently proposed the use of the term 'microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS)' to describe the specific type of acute respiratory distress syndrome seen in patients affected by SARS-CoV-2 [2]. After a multidisciplinary assessment of > 850 COVID-19 patients admitted to our Hospital with several bilateral pneumonia, we have collected evidences supporting a key role of vascular inflammation and microthrombosis in the pathophysiology of the multisystemic clinical manifestations that have been associated with COVID-19, including the heterogeneous cutaneous findings.

This seems to emerge also from the results of autoptic studies on patients affected by SARS-CoV-2. While a picture of diffuse alveolar damage with capillary congestion, microthrombi and hyaline membrane has been reported in lung tissues [3], signs of endothelial dysfunction and microthrombosis are also present in several extrapulmonary organs; in many cases, the patients did not have any evidence of macro and/or micro-thrombosis before death [4].

To further stress the possibility of a procoagulative state in these patients, some authors have reported the association between a significant elevation of D-dimer and mortality [5]; others have suggested the presence of diffuse complement mediated thrombotic microangiopathy, raising the question about the use of complement inhibitors in critically ill COVID-19 patients [6].

Despite the many controversial points, there is now a general consensus on the recommendation of anticoagulation in patient with severe SARS-CoV-2 infections [7]. Most authors and scientific international societies suggest the use of heparin. In addition to its antiinflammatory effect, heparin does not interact with several experimental drugs used for the treatment of SARS-CoV-2, alike other anticoagulants as the dicumarolic agent and the non-vitamin K antagonist oral anticoagulants. However, the dose of the prophylaxis and even the choice between a prophylactic and a treatment regimen remains controversial [8].

The International Society for Thrombosis and Hemostasis (ISTH) suggests the use of low molecular weight at the already recognized doses for deep venous thrombosis prophylaxis in adults [9]. In contrast, other centers propose to administer a higher prophylactic dose (double dose) in patients critically ill, after the report of an incidence of thrombotic event in intensive care unit patients as high as 31%, despite regular prophylactic anticoagulation [10]. Finally, others clinician recommend therapeutic anticoagulation in patients with severe SARS-CoV-2 infection [5]. The rational to start this more aggressive management, however, remains unclear and based on small retrospective series [7].

Randomized controlled trials are urgently needed to help clarifying the many therapeutic challenges associated with the management of SARS-CoV-2 patients.

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