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Editorial

COVID-19-ассоциированный тромбовоспалительный статус: гипотеза MicroCLOTS и ее перспективы (редакционная статья)

П. Нарделли[1], Дж. Ландони[1,2]

[1] Отделение анестезиологии-реаниматологии, Научно-исследовательский институт San Raffaele, Милан, Италия
[2] Университет Vita-Salute San Raffaele, Милан, Италия

COVID-19-Related Thromboinflammatory Status: MicroCLOTS and Beyond (Editorial)

Pasquale Nardelli[1], Giovanni Landoni[1,2]

[1] Anesthesia and Intensive Care Department, IRCCS San Raffaele Scientific Institute, Milan, Italy
[2] Vita-Salute San Raffaele University, Milan, Italy

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The COVID-19 global pandemic, infecting over 3.5 million people and killing over a quarter of a million in the first 4 months of 2020 [1], required physicians all over the world to suddenly face a completely new nosological identity, with unknown characteristics and clinical challenges.

Italy was the first Western country hardly hit by the epidemic, with the region of Milan being in the epicenter of the phenomenon. San Raffaele Scientific Institute was one of the first centers to organize an all-out response to the virus [2]. Our multidisciplinary scientific team was the first to hypothesize and publish a theory about acute respiratory distress syndrome (ARDS) pathogenesis in COVID-19, accounting for the peculiar clinical and radiological presentation [3]. The syndrome was called MicroCLOTS (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome): the replication of SARS-CoV-2 in cells expressing the surface receptor angiotensin-converting enzyme 2 (ACE2) may stimulate innate immune responses and complement activation, causing a massive local release of pro-inflammatory cytokines ultimately resulting in severe tissue injury and microvascular thrombosis.

As cells expressing ACE2 include lung epithelial cells, but also arterial and venous endothelial cells and arterial smooth muscle cells of multiple organs [4], MicroCLOTS theory may explain also the high incidence of both venous and arterial thromboembolism in COVID-19 patients. In fact, up to 1/3 of critically ill patients with COVID-19 appears to develop thrombotic complications [5] in spite of adequate thromboprophylaxis protocols. Thromboembolic complication ranged from deep venous thrombosis to ischemic stroke to the detection of thrombi in the lungs.

The presence of MicroCLOTS in the lungs may also explain the inefficacy or even the harm of high PEEP ventilation and excessive negative fluid balance, which are constricting pulmonary arterioles already partially obstructed by clots

Renal involvement also has a major role in COVID19: preliminary reports from Wuhan, China indicate that acute kidney injury occurred in 25 to 29 percent of critically ill patients [6, 7]. While Western world data on this topic are still lacking, the issue is being investigated [8]: autopsies reported peritubular erythrocyte aggregation and glomerular fibrin thrombi with ischemic collapse in kidneys of deceased COVID19 patients [9], possibly implying a similar etiology to pulmonary MicroCLOTS.

Managing a wide range of COVID-19 patients over the last two months, it appears we've being two different entities: an inflammatory phase, which responds well when targeting interleukins [10, 11] or complement [12] and a thrombotic phase which seems to respond well to thromboprophylaxis with low molecular weight heparin started early (at home or at hospital arrival) and to full anticoagulation in intensive care unit patients [13] and in selected patients in the main wards.

Адрес для корреспонденции:

Дж. Ландони
E-mail: landoni.giovanni@hsr.it

Correspondence to:

Giovanni Landoni
E-mail: landoni.giovanni@hsr.it

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