Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): a new variant of thrombotic microangiopathy?

Larisa Bobrova, Natalia Kozlovskaya, Yulia Korotchaeva, Irina Bobkova, Elena Kamyshova and Sergey Moiseev

To the Editor: In a recent article, Ciceri and colleagues[1] suggested that in a proportion of patients with coronavirus disease 2019 (COVID-19) "alveolar viral damage is followed by an inflammatory reaction and by microvascular pulmonary thrombosis". The authors proposed a new term — microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS) — to define the mechanism of severe pulmonary COVID-19.[1] It seems that in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection we may face a new variant of thrombotic microangiopathy (TMA), which, unlike the classic TMA, is associated with the activation of both primary haemostasis (platelet plug) and secondary haemostasis (plasma coagulation cascade), affecting foremost the pulmonary microvascular bed. The similar predominant damage of one organ (the kidney) is typical for the Shigatoxin-producing *Escherichia coli* haemolytic–uraemic syndrome.[2]

SARS-CoV-2 that replicates primary in human airway epithelial cells may trigger the cascade of events leading to endothelial damage followed by microthrombosis in the lung vessels and a generalised thrombotic microvascular injury of various vascular beds. The coagulation cascade activation may be due to virus-induced diffuse endothelial inflammation (endotheliitis),[3] induction of pro-inflammatory cytokine synthesis (tumour necrosis factor, interleukin [IL]-6 and IL-1β) with the development of cytokine storm,[4] and activation of the alternative and lectin complement pathways.[5]

Is it possible to predict the development of-TMA/MicroCLOTS? Cicero and colleagues suggest that some individuals may have a higher risk of alveolar viral damage with thromboinflammatory reaction, although they do not specify the determinants of this individual predisposition. We cannot not exclude that functional genetic polymorphisms in cytokine genes and complement system genes (similar to atypical haemolytic–uraemic syndrome) may contribute to the development of TMA/MicroCLOTS.

Possible mechanisms of COVID-19-associated lung injury, including inflammation and thrombosis with the development of TMA, justify the early administration of heparins, probably in combination with transfusions of fresh frozen plasma (similar to the treatment of other TMA variants). The latter contains natural anticoagulants, ADAMTS 13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13), which controls the excessive platelet thrombus formation, and proteins, which inhibit the activity of complement. We suggest that the use of fresh frozen plasma may limit SARS-CoV-2-associated thromboinflammatory syndrome.

Competing interests

None declared.

Author details

Larisa Bobrova[1]
Natalia Kozlovskaya[2]
Yulia Korotchaeva[1]
Irina Bobkova[1]
Elena Kamyshova[1]
Sergey Moiseev[1]

1 Sechenov First Moscow State Medical University, Moscow, Russian Federation
2 Peoples' Friendship University of Russia, Moscow, Russian Federation

***Correspondence*:** kamyshova-es@yandex.ru

References

1 Ciceri F, Beretta L, Scandroglio AM, et al. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. *Crit Care Resusc* 2020; 22: 95-7.
2 Jokiranta TS. HUS and atypical HUS. *Blood* 2017; 129: 2847-56.
3 Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; 395: 1417-8.
4 Liu J, Li S, Liu J, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine* 2020; 55: 102763.
5 Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. *Transl Res* 2020; 220: 1-13.