Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Could antiphospholipid antibodies contribute to coagulopathy in COVID-19?

To the Editor: We read with great interest the article by Manalo et al.[1] Coronavirus disease 2019 (COVID-19) patients may develop a thrombophilic state, and extensive microthrombosis has been found at autoptic examination in numerous organs.[2] We agree with Manalo et al[1] that it is likely that this phenomenon does not spare the skin, where it plausibly expresses itself through livedo reticularis and acral ischemia.[1,2] Hypercoagulability in COVID-19 patients should not be underestimated because in the worst-case scenario it may lead to death by causing pulmonary embolism or disseminated intravascular coagulation.[2] The pathogenesis underlying thrombophilia in COVID-19 patients is not clear yet. A recent report described 3 cases of Chinese patients affected by COVID-19 who had coagulopathy and antiphospholipid antibodies.[3] Indeed, livedo reticularis and acral ischemia can be observed in antiphospholipid syndrome. Disseminated intravascular coagulation also may be substantially indistinguishable from the most severe form of antiphospholipid syndrome; namely, catastrophic antiphospholipid syndrome, in which a "thrombotic storm" affects 3 or more organs or systems simultaneously, leading to multiorgan failure.[4] Zhang et al[3] cautioned that this might be a fortuitous coincidence because antiphospholipid antibodies may arise transiently in patients with critical illness and various infections. Moreover, the presence of these antibodies may rarely lead to thrombotic events that are difficult to differentiate from other causes of multifocal thrombosis in critically patients, such as disseminated intravascular coagulation, heparin-induced thrombocytopenia, and thrombotic microangiopathy.[3]

Nonetheless, antiphospholipid syndrome often arises after infectious triggers.[4] Viral induction of autoimmunity can be explained by various phenomena, including epitope spreading, molecular mimicry, cryptic antigen, and bystander activation.[5] Remarkably, greater than one-third of the immunogenic proteins in severe acute respiratory syndrome corona virus 2 have potentially problematic homology to proteins that are key to the human adaptive immune system.[5] Moreover, severe acute respiratory syndrome corona virus 2 seems to induce organ injury through alternative mechanisms beyond direct viral infection, including immunologic injury.[2]

Could antiphospholipid antibodies play a role in inducing coagulopathy in COVID-19 patients? Is coagulopathy in COVID-19 patients a manifestation of mild to very severe forms of antiphospholipid syndrome?

This is could be a far-fetched hypothesis but perhaps worth perusing to better understand the pathologic mechanisms underlying the very dangerous coagulopathy observed in COVID-19 patients. Moreover, antiphospholipid antibody testing is simple, rapid, and easily accessible. Further studies are needed to investigate the validity of this hypothesis and its possible clinical implications on anticoagulant therapy management in COVID-19 patients.

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REFERENCES

1. Manalo IF, Smith MK, Cheeley J, Jacobs R. A dermatologic manifestation of COVID-19: transient livedo reticularis. *J Am Acad Dermatol*. 2020;83(2):700.
2. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acro-ischemia. *Zhonghua Xue Ye Xue Za Zhi*. 2020; 41(0):E006.
3. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and antiphospholipid antibodies in patients with COVID-19. *N Engl J Med*. 2020;382(17):e38.
4. Linnemann B. Antiphospholipid syndrome - an update. *Vasa*. 2018;47(6):451-464.
5. Lyons-Weiler J. Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. *J Transl Autoimmun*. 2020;3:100051.

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