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.

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Covid-19 and in situ pulmonary artery thrombosis

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To the Editor,

The thrombogenic potential of Covid-19 is recognised and we read with interest the case series of 22 patients presented by Mueller-Peltzer and colleagues [1]. Their findings of pulmonary artery thrombi located within opacitated lung segments supports local clot formation. We would like to share our experience from the United Kingdom which adds impetus to the growing concept of in situ pulmonary artery thrombosis (PAT).

We studied 15 Covid-19 patients diagnosed with PAT following computed tomography pulmonary angiogram (CTPA) [2]. 12 out of 15 patients (80%) had non-resolving fever and dyspnoea for 7 days or more prior to hospitalisation. 7 (47%) required continuous positive airway pressure, 2 (13%) of which were subsequently intubated. All patients had significantly raised D-dimer, lactate dehydrogenase, C-reactive protein, ferritin and prothrombin times. Distribution of thrombosis correlated with the pattern of consolidation observed on CTPA in 9 (60%) patients; the majority being peripheral or subsegmental ($N = 14$, 93%) and only 1 central artery occlusion. No patients had clinical evidence of deep vein thrombosis.

Our study suggests that patients with acute deterioration, protracted course of illness (non-resolving symptoms), persistent oxygen requirements or significantly raised D-dimer should be investigated for PAT.

Clearly, the development of in situ immune-mediated PAT (perhaps a more accurate nomenclature) within the context of Covid-19 is a contributory factor to the pathogenesis of type 1 respiratory failure and need for mechanical ventilation. Sites of thrombosis correlating with areas of pulmonary infiltration suggests clot development may be related to underlying anatomically localised infective or inflammatory processes. The pattern of prothrombotic coagulopathy deviates from that of sepsis where thrombocytopenia is common and from disseminated intravascular coagulation where deranged clotting times are accompanied by a haemorrhagic tendency [3].

Thrombogenicity may occur in several ways. Upregulation of angiotensin II (consequent to viral-angiotensin converting enzyme 2 binding) has been mentioned in the potential pathophysiological mechanism of cytokine storm through dysregulation of the renin-angiotensin-aldosterone system and expression of interleukin-6, a key pro-inflammatory and pro-thrombotic cytokine [4–6]. Inflammation induced alveolar injury and hypoxaemia can further amplify the vascular endothelial response and augment thrombus formation [7].

Combined emerging evidence does indeed support the hypothesis that PAT originates locally or in situ. Conventional thromboprophylaxis dosing regimens may be inadequate and there seems an urgency for consensus agreement on enhanced prophylaxis in Covid-19 patients.

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Declaration of competing interest

No potential conflict of interest was reported by the authors.

References

[1] K. Mueller-Peltzer, T. Krauss, M. Benndorf, et al., Pulmonary artery thrombi are co-located with opacifications in SARS-CoV2 induced ARDS [published online ahead of print, 2020 Sep 11], Respir. Med. 172 (2020) 106135.
[2] J. Kho, A. Ioannou, K. Van den Abbeele, et al., Pulmonary embolism in COVID-19: clinical characteristics and cardiac implications, Am. J. Emerg. Med. (2020), https://doi.org/10.1016/j.ajem.2020.07.054.
[3] M. Ranucci, A. Ballotta, U. Di Dedda, E. Bayshnikova, M. Dei Poli, M. Resta, M. Falco, G. Albano, L. Menicanti, The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome, J. Thromb. Haemostasis. 18 (2020) 1747–1751, https://doi.org/10.1111/jth.14854.
[4] R.A. Fraga-Silva, B.S. Sorg, M. Wankhede, C. Dedeugd, J.Y. Jun, M.B. Baker, et al., ACE2 activation promotes antithrombotic activity, Mol. Med. 16 (5–6) (2010) 210–215.
[5] H. Li, L. Liu, D. Zhang, J. Xu, H. Dai, N. Tang, et al., SARS-CoV-2 and viral sepsis: observations and hypotheses, Lancet. 395 (10235) (2020) 1517–1520.
[6] B. Schieffer, E. Schieffer, D. Hilfiker-Kleiner, A. Hilfiker, P.T. Kovanen, M. Kaartinen, et al., Expression of angiotensin II and interleukin 6 in human coronary atherosclerotic plaques: potential implications for inflammation and plaque instability, Circulation. 101 (12) (2000) 1372–1378.
[7] N. Gupta, Y.Y. Zhao, C.E. Evans, The stimulation of thrombosis by hypoxia, Thromb. Res. 181 (2019) 77–83.

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