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Letter to the Editors-in-Chief

Arterial and venous thromboembolic disease in a patient with COVID-19: A case report

Dear Editors,

We read with great interest the study of Klok et al. [1], about the sky-high (31%) incidence of thrombotic complications despite thromboprophylaxis in ICU patients with COVID-19, and the letter by Rotzinger et al. [2], about their plea to perform a CT pulmonary angiography (CTPA) instead of a non-contrast chest CT in patients with respiratory deterioration or elevated D-dimer levels. While both articles are interesting and further generate hypotheses about the causal role of pulmonary embolism (PE) in clinical worsening of patients with COVID-19, we would like to take a moment to reflect on their papers, with an intriguing case presentation that highlights and further substantiates several key points.

We describe a patient with COVID-19 who consecutively developed an arterial (ischemic stroke) and venous thromboembolic event (PE) despite thromboprophylaxis with low molecular weight heparin (LMWH), following treatment for ischemic stroke with intravenous rt-PA (alteplase) and clopidogrel. On top of that PE was diagnosed after two previously performed CTPA imaging studies were negative.

1. Case presentation

A 57-year-old male with a history of peripheral arterial disease (PAD) presented to the emergency department with progressive cough, dyspnea, thoracic pain, headache and fever for 5 days. Vital signs revealed hypertension (150/70 mmHg), tachycardia (110 bpm), hypoxia (SpO2 of 87% at ambient air, respiratory rate: 16/min), and fever (40 °C). Laboratory results were notable for d-dimer (908 μg/L), lactate dehydrogenase (585 U/L) and C-reactive protein (78 mg/L). Because of thoracic pain, tachycardia and an elevated d-dimer level, CTPA, instead of a non-contrast chest CT in patients with thoracic pain, headache and fever for 5 days. Vital signs revealed hypotension (150/70 mmHg), tachycardia (110 bpm), hypoxia (SpO2 of 87% at ambient air, respiratory rate: 16/min), and fever (40 °C). Laboratory results were notable for d-dimer (908 μg/L), lactate dehydrogenase (585 U/L) and C-reactive protein (78 mg/L). Because of thoracic pain, tachycardia and an elevated d-dimer level, CTPA, instead of a non-contrast chest CT in patients with thoracic pain, headache and fever for 5 days. Vital signs revealed hypotension (150/70 mmHg), tachycardia (110 bpm), hypoxia (SpO2 of 87% at ambient air, respiratory rate: 16/min), and fever (40 °C). Laboratory results were notable for d-dimer (908 μg/L), lactate dehydrogenase (585 U/L) and C-reactive protein (78 mg/L). Because of thoracic pain, tachycardia and an elevated d-dimer level, CTPA, instead of a non-contrast chest CT in patients with thoracic pain, headache and fever for 5 days. Vital signs revealed hypotension (150/70 mmHg), tachycardia (110 bpm), hypoxia (SpO2 of 87% at ambient air, respiratory rate: 16/min), and fever (40 °C). Laboratory results were notable for d-dimer (908 μg/L), lactate dehydrogenase (585 U/L) and C-reactive protein (78 mg/L). Because of thoracic pain, tachycardia and an elevated d-dimer level, CTPA, instead of a non-contrast chest CT in patients with thoracic pain, headache and fever for 5 days. Vital signs revealed hypotension (150/70 mmHg), tachycardia (110 bpm), hypoxia (SpO2 of 87% at ambient air, respiratory rate: 16/min), and fever (40 °C). Laboratory results were notable for d-dimer (908 μg/L), lactate dehydrogenase (585 U/L) and C-reactive protein (78 mg/L). Because of thoracic pain, tachycardia and an elevated d-dimer level, CTPA, instead of a non-contrast chest CT in patients with

Second, it also shows the diagnostic challenges in patients with COVID-19, and in particular those who deteriorate rapidly. The impossibility to differentiate between respiratory failure due to progression of lung-tissue related abnormalities such as ground glass opacities or ARDS on the one hand and PE on the other hand is unprecedented. Where normally an alternative diagnosis is rather reassuring and actually reduces the risk of concurrent PE, in patients with COVID-19 this is at least questionable. In fact, our case shows that both, progression of COVID-related abnormalities and PE, can occur simultaneously or in a very short time frame. Eventually, repeated d-dimer (> 10,000 μg/L) was decisive to perform CTPA a third time. A report of the National Institute of Public Health for the Netherlands (RIVM) suggests that the combination of d-dimer levels increasing progressively and clinical worsening is suggestive for PE [6]. D-dimer elevations also have already been associated with poor

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prognosis [7]. Therefore, we believe that CTPA should be considered at a low threshold in patients with unexplained respiratory deterioration, certainly when d-dimer levels have increased progressively. In retrospect, we could have performed compression ultrasonography of the legs (CUS) before proceeding to the second or third CTPA [8]. If CUS would have been positive, an indication for anticoagulant therapy would be present already and another CTPA could have been avoided. It also would have helped in fully understanding the course of events, although deep vein thrombosis is lacking in the majority of patients [9].

In summary, this case highlights hypercoagulability as a major contributor to COVID-19 related complications and suggests that commonly used diagnostic and therapeutic approaches may be insufficient to ameliorate the risk of thromboembolic events, underscoring the need to remain vigilant for the occurrence of these events in patients with COVID-19.

Fig. 1. CT scans of the chest.
(A) High resolution chest CT scan performed at admission, showing ground-glass abnormalities with and without reticulation (“crazy paving”) with a predominantly peripheral distribution, consistent with COVID-19-related pneumonia.
(B) CTPA performed at admission that did not reveal signs of pulmonary emboli.
(C) High resolution chest CT scan performed on day 2, showing a marked increase in COVID-19-related pulmonary involvement and new areas of consolidation.
(D) CTPA performed on day 2, again showing no signs of pulmonary embolism.
(E) High resolution chest CT scan performed on day 7, showing improvement of COVID-19-related pulmonary changes with less extensive abnormalities and signs compatible with organising pneumonia.
(F) CTPA performed on day 7, showing lobar (arrow) and subsegmental (not shown) pulmonary emboli.
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Declaration of competing interest

The authors have declared no conflicts of interest.

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