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CHEST

Extensive DVT and Pulmonary Embolism Leading to the Diagnosis of Coronavirus Disease 2019 in the Absence of Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia

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There is growing evidence that coronavirus disease 2019 (COVID-19) is associated with a hypercoagulable state. To date, all patients reported with venous thromboembolic disease and COVID-19 have shown evidence of viral pneumonia. Here, we report the case of a 31-year-old patient with unexplained extensive DVT and bilateral pulmonary embolism in the absence of COVID-19 pneumonia, leading to the diagnosis of otherwise asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In the context of the COVID-19 pandemic, given the high rates of otherwise asymptomatic patients, testing for SARS-CoV-2 should be performed in all patients with unexplained VTE occurring in COVID-19-endemic areas, even in the absence of other disease manifestations suggestive of SARS-CoV-2 infection.

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KEY WORDS: acute pulmonary embolism; coronavirus disease 2019; venous thromboembolic disease

Case Report

A 31-year-old patient with no past medical history presented to the ED for an erythematous swelling of the left inferior limb. The patient had no fever, stable hemodynamic status, and oxygen saturation was 99% (room air). Notably, the heart rate was 133 beats/min. Blood tests showed high inflammatory markers with C-reactive protein, ferritin, and fibrinogen levels of 225 mg/L, 2646 μg/L, and 7.22 g/L, respectively. Moreover, the D-dimer level was 5.0 mg/L. CT venography showed an extended femoropopliteal DVT expanding to the subrenal vena cava, and a lobar bilateral pulmonary embolism (Fig 1). There was no sign of coronavirus 2019 disease (COVID-19) pneumonia, nor evidence of solid or hematologic malignancy. The patient had no risk factors and no familial history of VTE. The etiologic workup (including the search for protein C, protein S, and antithrombin deficiencies, factor II and V mutations, antiphospholipids, and lupus anticoagulant) produced negative results. Owing to unexplained (despite VTE) high inflammatory parameters, and given the context of epidemic COVID-19 (estimated proportion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected among the inhabitants of the Paris area at the time of patient treatment: 9%; range, 6%-14%)[1] and the high rates of asymptomatic patients (up to 56% within

ABBREVIATIONS: COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

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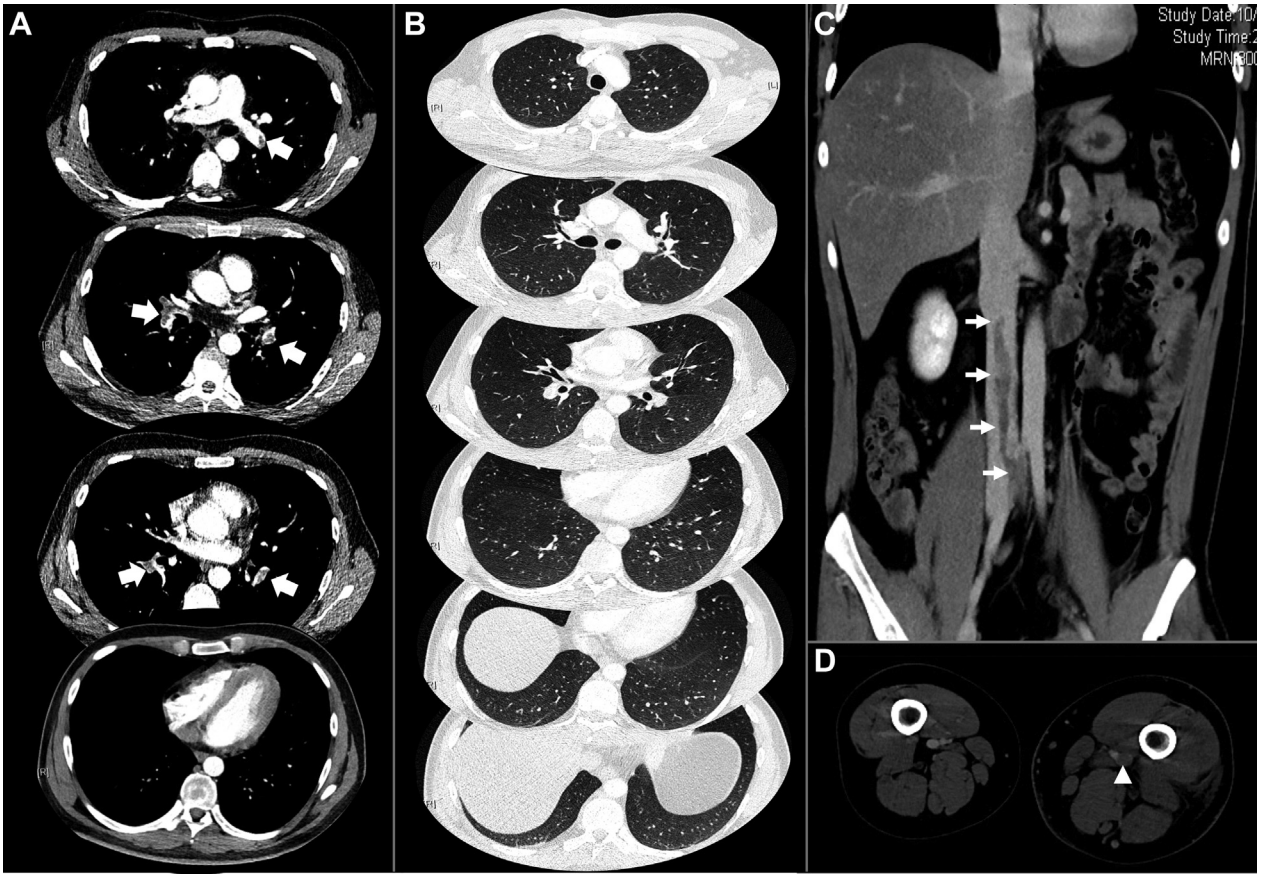

Figure 1 – *A-D, CT pulmonary angiography and venography showing multiple troncular, lobar, and segmental thrombi (arrows) (A); normal lung parenchyma (B); extensive thrombus of the lower vena cava (arrows) (C); and enlargement of the left leg with femoral venous thrombosis (arrowhead) (D).*

studies),[2-5] real-time polymerase chain reaction for SARS-CoV-2 was performed on a nasopharyngeal swab and tested positive. The patient had no acute respiratory; ear, nose, and throat; or neurologic or digestive symptoms suggestive of COVID-19 infection. At most, he had presented mild symptoms of bronchitis a week before hospitalization. The patient was transferred to another unit dedicated to the treatment of patients with COVID-19, and his condition improved with low-molecular-weight heparin therapy (subcutaneous enoxaparin; starting dose, 9,000 IU bid; subsequently increased to 12,000 IU bid after monitoring of anti-Xa activity). Seven days after admission, the patient was discharged with normal clinical parameters and no new COVID-19-related symptoms.

Discussion

Both venous and arterial thromboses have been reported in patients infected with betacoronaviruses.[6] In a retrospective analysis of 199 confirmed SARS-CoV-1 cases in Singapore, 18 episodes of VTE were reported and, in the same institution, postmortem autopsies of eight patients reported pulmonary embolism in four patients.[7,8] Although less extensively reported, Middle East respiratory syndrome coronavirus also seems to be associated with a procoagulant state.[9] Recently, Danzi et al[10] first reported the case of a patient with severe COVID-19 pneumonia and concomitant bilateral pulmonary embolism in the absence of predisposing factors for acute VTE. Moreover, within case series, the rates of COVID-19-related DVT and acute pulmonary embolism are as high as 31% and 21%, respectively.[11-15] Hence, some authors suggested that CT pulmonary angiography (rather than a chest CT scan) be performed in all patients with COVID-19 requiring hospitalization and/or in case of respiratory worsening.[13]

To date, to the best of our knowledge, all cases of VTE occurring during the course of betacoronavirus infections had concomitant evidence of viral pneumonia. The coexistence of VTE and other viral (eg, cytomegalovirus or

parvovirus B19) infections has seldom been depicted, yet the causal link remains debated.[16] Conversely, the pathophysiology of COVID-19-related thrombosis seems peculiar, with SARS-CoV-2-induced inflammation and endotheliopathy being prominent features contributing to the very high rates of VTE in this setting.[17] Moreover, the presence of lupus anticoagulant has also been reported, yet its pathogenic role is unclear at this point.[18] From a biological standpoint, high D-dimer levels, high fibrin degradation products, and prolonged prothrombin time could be associated with poorer outcomes.[19] Of note, the patient's D-dimer level was superior to the threshold of 3.0 mg/L, which provided sensitivity, specificity, and negative predictive values of 76.9%, 94.9%, and 92.5% in the study by Cui et al[12] for the diagnosis of VTE in the ICU.

In conclusion, although we cannot preclude that VTE was related to another cause than viral infection and that the coexistence of both conditions was merely fortuitous, this case suggests that testing for SARS-CoV-2 should be performed in all patients with unexplained VTE occurring in COVID-19-endemic areas, even in the absence of other disease manifestations suggestive of SARS-CoV-2 infection.

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