CASE REPORT

Coronavirus Disease-2019 Pneumonia and Pulmonary Embolism: Presentation of Four Cases

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Abstract

Since the beginning of the Coronavirus Disease-2019 (COVID-19) outbreak, elevated D-dimer levels as an acute-phase reactant have been reported in some patients. Additionally, the patients with pneumonia are at increased risk of developing thromboembolic events. Diagnosing acute pulmonary embolism and deep vein thrombosis can be challenging in SARS-CoV2–positive patients. Here, we report four patients with COVID-19 pneumonia to highlight the possibility of acute thromboembolism in these patients. The physicians should be aware of this complication and even consider prophylactic anticoagulant therapy in proper clinical settings.

Keywords: Acute pulmonary embolism, COVID-19, D-dimer levels.

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Introduction

In December 2019, cases of pneumonia of unknown cause were reported in Wuhan city, China. Soon after, the causative agent was found to be SARS-CoV2.[1,2] The outbreak of the disease, known as Coronavirus Disease-2019 (COVID-19), was declared a pandemic in March 2020.

An elevated D-dimer is generally considered to be associated with deep vein thrombosis (DVT) and acute pulmonary embolism (APE).[3] However, increased D-dimer levels have been reported with other conditions, such as advanced age, pregnancy, malignancies, inflammatory processes, and peripheral arterial diseases[4–6] During the COVID-19 pandemic, elevated levels of D-dimer have been reported in some patients, even without evident DVT or APE.[7,8]

Here, we report four different patients from Isfahan, Iran, with acute APE and reverse transcription polymerase chain reaction (RT-PCR)–confirmed COVID-19 infection.

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Case Descriptions

Case 1

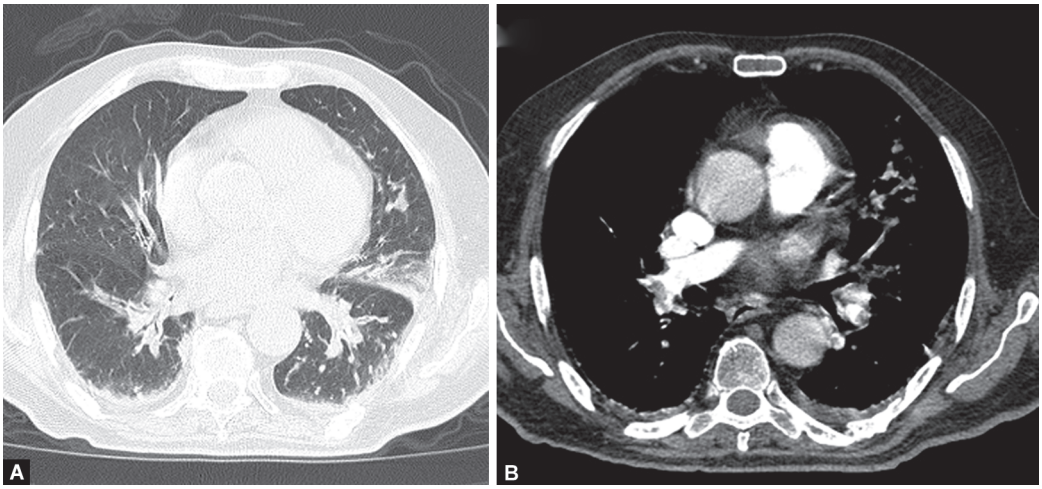
Figure 1 illustrates the case of an 86-year-old male admitted to our hospital with fever, cough, and dyspnea. He was hospitalized for 10 days. On admission his blood tests showed a white blood cell (WBC) count of 10.30 (10^3/μL) with 69.4% neutrophils and 20.7% lymphocytes, a platelet count of 490 (10^3/μL), an erythrocyte sedimentation rate (ESR) of 55 mm/hour, and a C-reactive protein (CRP) of 79 mg/L. On the third day of admission, the patient underwent pulmonary computed tomography (CT) angiography and lower limb compression ultrasonography due to deterioration in his clinical condition and elevated D-dimer levels (14,496 ng/mL). The lower limb compression ultrasound was negative, but his CT angiography revealed bilateral filling defects within the lobar and segmental branches of the pulmonary artery diagnostic for APE.

Case 2

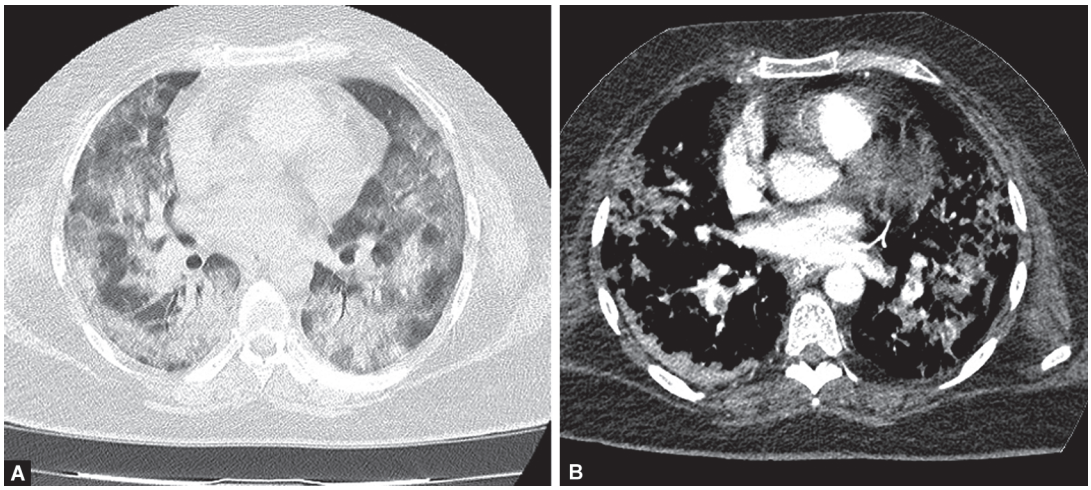
Figure 2 depicts the case of a 42-year-old female admitted to our hospital for 33 days. On admission, she had fever, dyspnea, cough, and diarrhea. Increased values of CRP (141 mg/L), ESR (93 mm/hour), and D-dimer (806 ng/mL) were present. Her blood test also revealed a WBC count of 10.60 (10^3/μL) with a 9.2% lymphocytes (i.e., lymphocytopenia). Initially, the patient was receiving supportive treatment, but subsequently she developed respiratory failure warranting implementation of mechanical ventilation and admission to intensive care unit (ICU). Nineteen days after admission, she underwent pulmonary CT angiography due to high clinical suspicion of APE and elevation in D-dimer levels (8,727 ng/mL). CT angiogram confirmed bilateral filling defects in segmental and sub-segmental branches of pulmonary artery.

Case 3

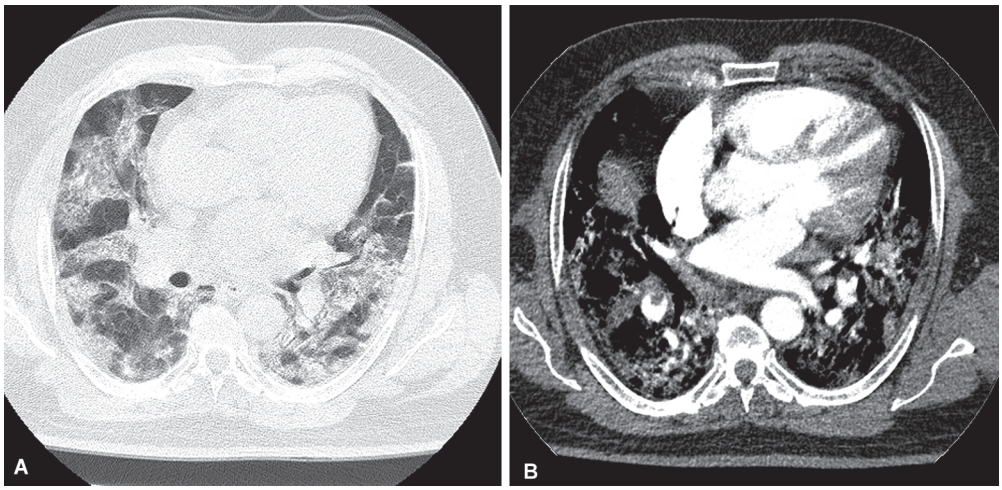
Figure 3 belongs to a 38-year-old man hospitalized for 13 days. He presented with progressive dyspnea. On admission, he had WBC count of 4.9 (10^3/μL) with 67% neutrophils and 24.1% lymphocytes, 120,000 platelets per micro liter, and elevated ESR (56 mm/hour) and CRP (58 mg/L). On the ninth day of admission, the patient became a candidate for pulmonary CT angiography because of lack of response to therapies and rising D-dimer levels (14,269 ng/mL on the sixth day vs >15,000 ng/mL on the eighth day). CT angiogram confirmed APE.



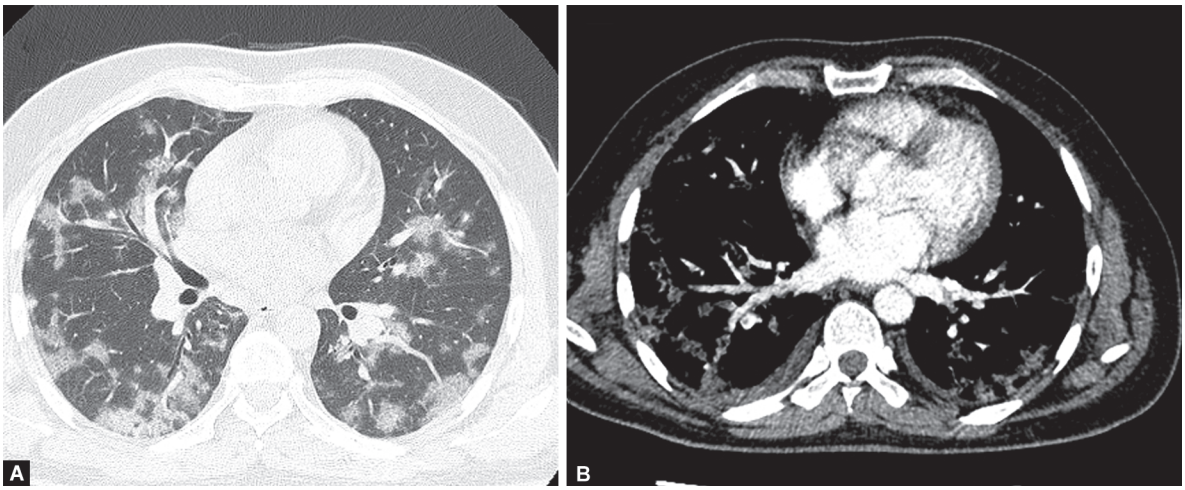
Figs 1A and B: Images of an 86-year-old man with COVID-19 pneumonia: (A) Axial unenhanced chest CT obtained at the day of admission showing areas of ground glass and reticular opacity; (B) Axial pulmonary CT angiography demonstrating bilateral filling defects in lobar and segmental branches of the pulmonary artery



Figs 2A and B: Images of a 42-year-old woman with COVID-19 pneumonia: (A) Axial unenhanced chest CT at the day of admission showing bilateral multilobar peripheral and peribronchovascular ground glass and consolidative opacities; (B) Axial pulmonary CT angiography confirming bilateral filling defects in segmental and subsegmental branches of the pulmonary artery



Figs 3A and B: Images of a 38-year-old man with COVID-19 pneumonia: (A) Axial unenhanced chest CT obtained at the first day of admission revealing bilateral ground glass opacities and areas of crazy paving; (B) Axial pulmonary CT angiogram showing filling defects in segmental branches of the pulmonary artery bilaterally



Figs 4A and B: Images of a 42-year-old man with COVID-19 pneumonia: (A) Axial unenhanced chest CT obtained at the first day of admission revealing bilateral ground glass opacities; (B) Axial pulmonary CT angiogram showing a filling defects in subsegmental branches of the pulmonary artery bilaterally

Case 4

Figure 4 shows the case of a 42-year-old-man admitted to hospital because of fatigue, fever, dyspnea, and cough. On the fourth day, he experienced progressively worsening dyspnea and elevated D-dimer levels (>15,000 ng/mL); thus, a pulmonary CT angiography was performed. Filling defects were evident within the subsegmental branches of pulmonary artery on both sides.

After established diagnosis of APE, treatment with standard therapeutic doses of anticoagulants (low-molecular-weight Heparin 1 mg/kg every 12 hours) was initiated for all four patients. All the patients did well except the third case who died of acute respiratory distress syndrome.

Discussion

Critically ill patients are at increased risk of thromboembolic events mainly due to immobility; it is also known that acute severe infections can lead to increased risk of thromboembolic events per se.[9] Previous studies have shown that patients with pneumonia are at two- to threefold increased risk of DVT.[10] Undiagnosed or untreated APE can pose higher mortality risks in these patients. An association has been suggested between influenza-induced pneumonia and procoagulant states.[11–13] APE has also been reported in one patient with severe acute respiratory syndrome (SARS).[14] However, to the best of our knowledge, no cases of APE and Middle East Respiratory Syndrome (MERS), the other coronavirus reported previously, have been record. Since the beginning of the COVID-19 pandemic, three case reports have been published pointing out a possible association between the novel coronavirus pneumonia and APE with or without DVT.[15–17] Evidences suggest that the coagulopathy associated with COVID-19 is a combination of low-grade DIC and localized microangiopathy.[18] It has also been suggested that there is an association between the inflammatory cascade and the coagulation cascade.[19] Taken together, it has been postulated that SARS-CoV2 can cause thrombosis formation.

Previous studies have reported elevated D-dimer levels in COVID-19 patients as a non-specific acute-phase reactant and baseline characteristic of critically ill patients.[20–23] Although relying simply on D-dimer levels to diagnose APE and DVT in COVID-19 patients may be misleading, elevated level of D-dimer has good negative-predictive value and can still be useful guide in management of critically ill patients with SARS-CoV2–induced pneumonia.

All our cases had higher-than-normal D-dimer levels, and none had recognized risk factors predisposing to thromboembolism except for decreased mobility and severe pneumonia. The present cases suggest that APE should be suspected in COVID-19 patients who follow a deteriorating course, and by clinical suspicion, pulmonary CT angiography should be conducted. In addition, the need is felt to find an optimal cutoff point value for D-dimer in SARS-CoV2–positive patients in order to diagnose DVT and APE with greater sensitivity and specificity. Consequently, the use of prophylactic doses of anticoagulants may be advocated.

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