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Severe Acute Proximal Pulmonary Embolism and COVID-19: A Word of Caution

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Acute pulmonary embolism is an uncharacteristic presentation in patients with coronavirus 2019 (COVID-19). Here we describe the case of a young woman presenting with severe pulmonary embolism, without any associated symptoms of infections. A clot in a patent foramen ovale was noted. Despite emergency surgical embolectomy, her clinical conditions continued to deteriorate. She was put on extracorporeal life support and tested positive for COVID-19. She died of multiorgan failure on day 10. COVID-19 may have a thrombogenic effect, and it may need to be considered in cases of pulmonary embolism and in the absence of any obvious risk factor.

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The recent coronavirus 2019 (COVID-19) pandemic is placing practitioners under the pressure to cope with the novel challenges it presents, in terms of clinical identification of the different symptoms of the pathology and testing of new or already known treatments.[1,2]

Much attention is dedicated to the potential COVID-19 has to cause acute lung injury and acute respiratory distress syndrome, but cases of acute pulmonary embolism in COVID-19 patients are also very recently described. Coincident pulmonary embolism has been detected on computed tomography (CT) scans of patients hospitalized mainly for infectious respiratory symptoms.[3,4] Here, we discuss the clinical case of a patient presenting with severe proximal pulmonary embolism, in the absence of pneumonia, and who, 9 days after her admission, tested positive for COVID-19.

A 45-year-old woman was admitted to our emergency department in the north of France. She had an active lifestyle, but had a body mass index of 40.4 kg/m^2, and was receiving hypertensive therapy (ramipril 5 mg per day). She was not receiving oral contraceptives. The patient complained of dyspnea and sore throat, without any associated fever or coughs for 1 week before admission to hospital and had taken ibuprofen as self-medication. On March 18, 2020, the day of her admission, she had chest pain, syncope, and tachypnea. Arterial blood gas measurements revealed Po_2 54 mm Hg and PCo_2 21 mm Hg. Her C-reactive protein level was 20 mg/L, and N-terminal prohormone B-type natriuretic peptide (NT-proBNP) was 11,021 pg/mL. Bedside transthoracic echocardiography showed left ventricular ejection fraction of 65% and a hypokinetic right ventricle (tricuspid annular plane systolic excursion 13 mm, S wave 8 cm/s) associated with severe systolic pulmonary hypertension (95 mm Hg). A patent foramen ovale was present with a large thrombus originating from the right atrium and extending to the left atrium. Contrast-enhanced CT scan showed massive bilateral proximal pulmonary embolism (Figure 1A, 1B). Because of the elevated risk of systemic embolism, thrombolysis was not considered.

The patient was transferred immediately to the operating room, and as per our routine practice in our center for these unstable patients, cardiopulmonary bypass was established under local anesthesia, by surgical cutdown of the femoral vessels at the level of the right groin. Surgical embolectomy was performed through median sternotomy after arresting the heart (Figure 1C, 1D). The patient's clinical condition stabilized during her first week in the intensive care unit. However, she had some degree of right heart failure, and despite administration of fluid resuscitation and vasopressors, she had persistent vasoplegic syndrome. Also, weaning from the ventilator was not possible. A Doppler peripheral echography revealed a deep venous thrombosis at the level of the left leg without any floating clot inside the inferior vena cava.

On day 8, she had severe hypoxemia refractory to maximum mechanical ventilation. She was put in a prone position for 16 hours, which improved gas blood oxygenation. On day 9, while remaining in the supine position, the patient had fever (42°C), hypoxemia (Po_2 54 mm Hg), and severe septic shock. Computed tomography scan was not done owing to her unstable clinical condition, but chest roentgenogram showed extensive bilateral interstitial infiltration (Figure 2). Transthoracic echocardiography was stable and showed no further impairment of right or left ventricular function. The patient was tested for COVID-19 at that time, and put on venous arterial extracorporeal life support as a rescue treatment (flow 6.4 L/min). Polymerase chain reaction test for COVID-19 was positive. The patient's clinical condition deteriorated rapidly, and she died of multiorgan failure on March 28, 2020, day 10 after embolectomy.

A post hoc analysis of the initial CT scan, made by the radiologists, found there were already slight bilateral interstitial ground-glass opacities compatible with COVID-19 lung parenchymal lesions (Figure 3).

Comment

COVID-19 related pathology has been constantly evolving during the past month. The association between acute pulmonary embolism and COVID-19 has been reported only in two very recent publications.[3,4] Unlike our

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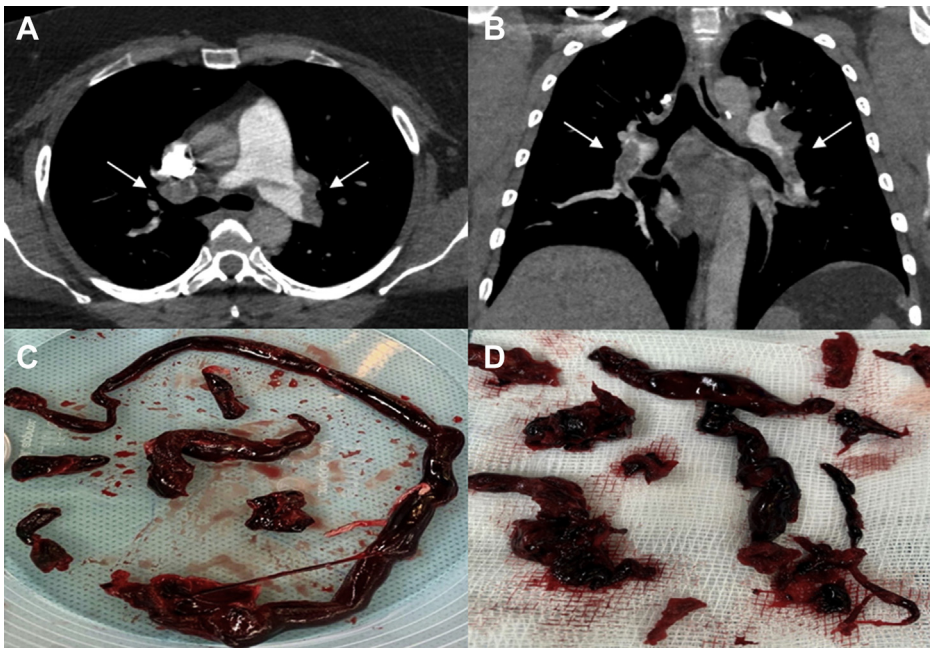

Figure 1. (A, B) Contrast-enhanced computed tomography scan shows proximal bilateral acute pulmonary embolism (arrows). (C, D) Numerous clots removed during surgery from right and left branches of the pulmonary artery.

patient whose clinical presentation was dominated by acute embolism, with no fever, cough, and muscular fatigue, in those publications pulmonary embolisms were diagnosed retrospectively on the CT scans of patients having COVID-19 "classic" infectious respiratory clinical presentation. Our patient was not identified as a potential COVID-19 patient and was not tested because her strong chest pain, syncope, and tachypnea were attributed to the acute proximal pulmonary embolism, and except for the dyspnea and sore throat, she did not have the symptoms usually associated with COVID-19.

The probability of a nosocomial COVID-19 infection during our patient's hospital stay is minimal as she remained intubated in sterile conditions in the intensive care unit with no member of the attending team testing positive or having any COVID-19 signs over this period. Moreover, a post hoc analysis indicated the initial CT scan already showed signs consistent with COVID-19 lung lesions.

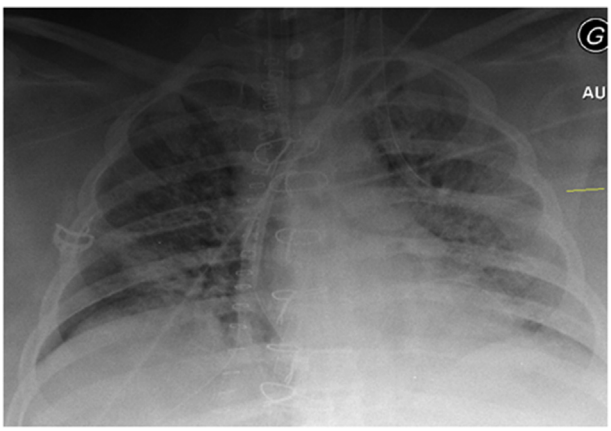

Figure 2. Chest roentgenogram showing bilateral interstitial lung lesions.

It is difficult to take a definite position on the role of treatment our patient received before her admission to the hospital. Angiotensin-converting enzyme 2 is a co-receptor for viral entry for SARS-CoV-2, and it may have a role in COVID-19 pathogenesis, although there is insufficient evidence to link angiotensin-converting enzyme inhibitors or renin-angiotensin system blockers to severe forms of COVID-19.[5,6] A similar uncertainty exists as to the role of the patient's ibuprofen oral intake and its potential relationship with severe forms of COVID-19.[7]

Although the evidence is insufficient to establish a firm association between pulmonary embolism and COVID-19, the latter may have a thrombogenic effect and eventually cause pulmonary embolism. Cases of pulmonary embolism were also noted during the coronavirus severe acute respiratory syndrome epidemic in 2003. Indeed, an underlying thrombophilic state, with frequent pulmonary embolisms in necropsy series of severe acute respiratory syndrome patients, was reported.[8]

In conclusion, we want to raise awareness that potentially COVID-19 and severe acute pulmonary embolism may be related, and in the absence of clear symptoms currently associated with this viral infection, the clinic may be totally dominated by the hemodynamic or respiratory symptoms of acute pulmonary embolism. For this reason, when presented with a patient with pulmonary embolism, without any evident risk factor for this pathology, the potential association between COVID-19 and pulmonary embolism should also be considered. If true, the early

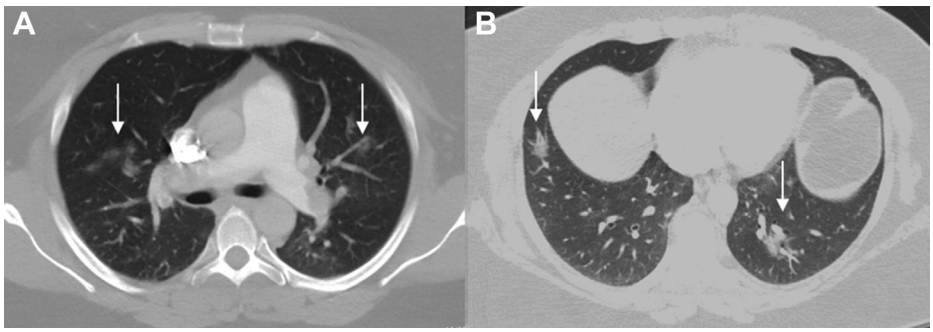

Figure 3. (A, B) Parenchymal windows of initial contrast-enhanced computed tomography scan showing bilateral interstitial ground-glass opacities (arrows).

detection of COVID-19 infection can lead to prompter and more aggressive systemic treatment, according to local recommendations or evaluation protocols.

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