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Bilateral Acute Cardioembolic Limb Ischemia After Coronavirus Disease 2019 Pneumonia in a Lung Transplant Recipient: A Case Report

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ABSTRACT

Very few cases of lung transplant patients affected by coronavirus disease 2019 (COVID-19) have been reported to date. A 31-year-old patient who underwent bilateral lung transplantation for cystic fibrosis in 2012 was admitted for severe acute lower limb pain. He had a confirmed exposure to COVID-19 and a 3-week history of upper respiratory tract infection. Whole-body computed tomography (CT) angiography revealed an occlusion of the 2 common femoral arteries. CT angiography detected an intracardiac thrombus in the left ventricle. Chest CT angiography showed ground-glass opacities consistent with COVID-19.

A bilateral femoral surgical embolectomy using Fogarty catheter was successfully performed. Specific reverse transcription polymerase chain reaction for severe acute respiratory syndrome coronavirus 2 performed on an extracted thrombus was negative, but IgM antibodies specific for COVID-19 were detected. Cardiac magnetic resonance imaging demonstrated a subendocardial and almost transmural late gadolinium enhancement in the mid and distal inferolateral and inferior wall segments, consistent with a nonrecent myocardial infarction and an apical centimetric thrombus adjacent to the lesion. Thrombophilia laboratory tests found the presence of a positive lupus anticoagulant.

Treatment with low-molecular-weight heparin and aspirin was prescribed. On day 13, the patient was discharged from the hospital.

This case underlines the need to be vigilant with respect to the thrombotic complications of COVID-19 and raises the issue of thrombosis prevention in COVID-19 patients.

IN late December 2019, the epidemic of a coronavirus disease 2019 (COVID-19) broke out in Wuhan, China, and then spread rapidly around the world. Although the clinical impact of the disease has been well described for immunocompetent patients, its consequences on populations treated with immunosuppressive (IS) drugs are still poorly understood, especially concerning solid organ transplant (SOT) recipients. Very few cases of lung transplant patients affected by COVID-19 have been reported to date [1].

This article describes the case of a young lung transplant patient with COVID-19 pneumonia, which was followed by acute limb ischemia. We hypothesize that this complication

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was secondary to a lupus anticoagulant-induced intracardiac thrombus.

CASE REPORT

A 31-year-old patient who had undergone double lung transplantation (LTx) for cystic fibrosis in 2012 was admitted to the emergency department for severe acute pain of the lower limbs. He had a known COVID-19 exposure. One month before this episode, the patient had a 3-week history of fever, fatigue, anorexia, weight loss, dyspnea, nausea, ageusia, and nasal obstruction, for which he had received at-home treatment with oseltamivir and cefuroxime. His main comorbidities were superior vena cava syndrome secondary to a thrombosis of a totally implantable venous access device prior to LTx and a chronic lung allograft dysfunction with a grade 2 bronchiolitis obliterans syndrome associated with mildly positive class II donor-specific antibodies. Regarding the high risk of rejection, the patient's IS treatment combined cyclosporin (150 mg twice daily), everolimus (0.75 mg twice daily), mycophenolate mofetil (1500 mg twice daily), and prednisone (10 mg/d) associated with azithromycin (250 mg 3 times/week).

In the emergency department, the patient reported painful and cold legs, loss of motricity, and sensitivity predominant on the right side. Right and left dorsalis pedis artery pulses were abolished.

Chest CT angiography showed bilateral consolidation areas and ground-glass opacities with basal and peripheral predominance, which was consistent with COVID-19 infection (Fig 1). No pulmonary embolism was observed. A venous Doppler ultrasound of the lower limbs and whole-body computed tomography (CT) angiography revealed a sharp and abrupt occlusion of the 2 common femoral arteries, a segmental thrombosis of the left internal iliac artery (Fig 2A), and an area of splenic infarction. Arteries were otherwise strictly normal. CT angiography detected an intracardiac thrombus (14 x 10 mm) in the left ventricle, which was later confirmed by transthoracic echocardiography. A nasopharyngeal swab using reverse transcription polymerase chain reaction tested negative for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Laboratory tests revealed increased platelet levels (536 G/L) and white blood cell counts (15.2 G/L), as well as mild anemia (9.5 g/dL)

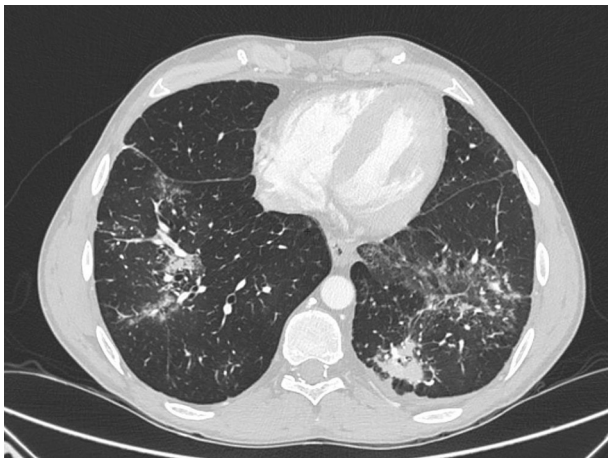


Fig 1. Pulmonary computed tomography showing patchy areas of consolidation and ground-glass opacities 1 month after COVID-19 respiratory symptoms onset.

and normal lymphocyte count (2.05 G/L). The troponin level was 0.038 ng/mL (normal range <0.01). D-dimer testing was not performed. Measurements of arterial blood gases showed normal pH, pO₂ of 192 mm Hg, and pCO₂ of 24 mm Hg at an O₂ flow rate of 2 L/min. The patient's creatinine level was 112 μmol/L (normal range 59-104 μmol/L), with normal liver function tests. The C-reactive protein level was normal as well, as were prothrombin and activated partial thromboplastin times, but the fibrinogen level was 6.72 g/L (normal range 2-4 g/L).

An emergency bilateral femoral surgical embolectomy using a Fogarty probe was successfully performed, which enabled extraction of white inflammatory-like thrombi from both sides. These were sent for specific reverse transcription polymerase chain reaction for SARS-CoV-2, which turned out to be negative. The same day, low-molecular-weight heparin was prescribed.

On day 2, the patient had fully recovered from acute limb ischemia and was transferred to the respiratory department for further care and treatment. A second nasopharyngeal swab testing was negative, but specific serology for SARS-CoV-2 confirmed COVID-19 with strongly positive IgM and mildly positive IgG levels, using rapid test Biosynex COVID-19 BSS (Strasbourg, France). This test showed good diagnostic performance during the current evaluation.

On day 6, an echocardiography was carried out to investigate the origin of the intracardiac thrombus. It revealed subnormal left ventricular ejection fraction and confirmed the presence of a 12 x 17 mm thrombus adjacent to an akinetic inferoapical segment, although no patent foramen ovale. Cardiac magnetic resonance imaging (MRI) demonstrated a subendocardial and almost transmural late gadolinium enhancement, with sharp margins, in the mid and distal inferolateral and inferior wall segments, which was consistent with myocardial infarction and not suggestive of COVID-19-related cardiac injury. The apical centimeter thrombus was adjacent to the lesion (Fig 2B). The electrocardiogram showed abnormal T waves in apical myocardium territory.

A large thrombophilia screening was performed and only revealed a positive lupus anticoagulant. Specific research for factor II, factor V, and JAK 2 mutations tested negative. The rest of the thrombophilia screening revealed an increased factor VIII (350%, normal range 60-150), but antithrombin III tested normal (106%, normal range >80), as well as protein C (118%, normal range >70) and protein S (97%, normal range >65). The lupus anticoagulant was, however, found negative in 2 serum samples previously collected in 2018 and 2019. A previous testing for antithrombin III performed routinely in 2019 was normal (101%).

Aspirin was added to low-molecular-weight heparin, which was then replaced by oral vitamin K-antagonist treatment. The IS regimen was not modified considering that infectious symptom onset occurred more than 1 month earlier, and the risk of rejection was considered important.

We did not observe any other clotting abnormality after the thrombectomy. On day 13, the patient was stable and discharged from hospital after a second echocardiography considered as unchanged (Fig 3).

DISCUSSION

The main COVID-19-related thrombotic manifestations described until now include pulmonary embolism, acute coronary syndrome, and stroke [2]. Several potential risk factors for thrombosis have been proposed, including hypoxemia, inflammation, and endothelial dysfunction.

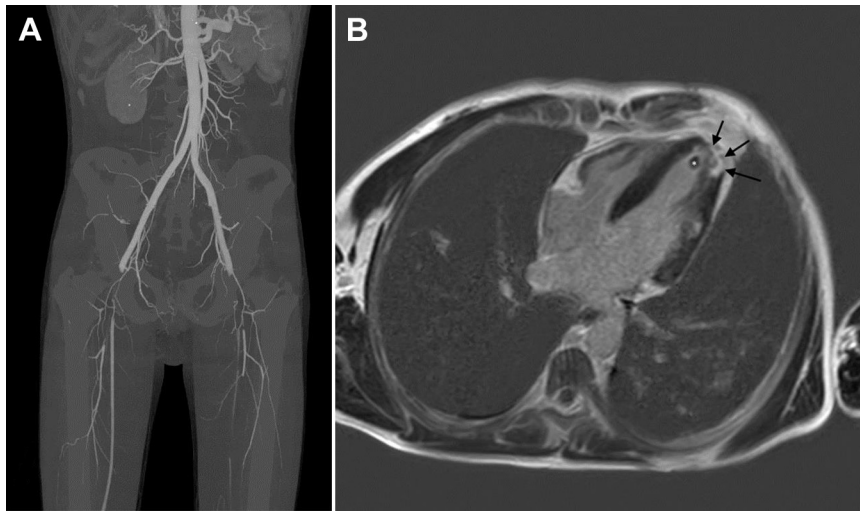


Fig 2. (A) Computed tomography angiography: sharp and abrupt occlusion of the 2 common femoral arteries, segmental thrombosis of the left internal iliac artery. (B) Cardiac magnetic resonance imaging: subendocardial and almost transmural late gadolinium enhancement, with sharp margins, in the mid and distal inferolateral and inferior walls, consistent with myocardial infarction (black arrows), and apical centimetric thrombus adjacent to the lesion (white star).

Lupus anticoagulant can arise transiently in patients with critical illness and various infections. Previous studies showed a high incidence in lupus anticoagulant in patients with severe COVID-19, and their role in the development of the coagulopathy requires further investigations [3,4].

Cardiac MRI demonstrated abnormalities characteristic of a nonrecent myocardial infarction. When and how this myocardial infarction occurred is still unclear. Indeed, echocardiography and electrocardiogram performed before LTx were normal. Retrospectively, the post-LTx electrocardiogram revealed abnormal T waves in the apical myocardial territory that were persisting so far, whereas 1-month post-LTx, echocardiography demonstrated no obvious abnormality. No further explorations were performed thereafter, considering the young age of our patient and absence of other cardiac comorbidity.

This case is remarkable because these arterial vascular complications occurred more than 1 month after the onset

of respiratory infectious symptoms and in a young patient without any known arterial peripheral comorbidity [5]. However, regarding his comorbidities and the elevated platelet count, we consider this patient at possible risk for thrombosis. This case underlines the need to be vigilant with respect to various thrombotic complications of COVID-19 and raises the issue of thrombosis prevention in SARS-CoV-2 patients.

Furthermore, the specific impact of IS treatment on COVID-19 severity is still not well defined. The specific care of SOT recipients during the COVID-19 epidemic was only the object of a few case reports, especially concerning IS treatment management [6–8]. When treating opportunistic viral infections in transplant patients, it is common to reduce or even suspend IS treatment to enable patients to reacquire anti-infection immunity and reduce the severity of symptoms [9]. Similar recommendations were proposed for COVID-19–infected transplant patients. In our case, IS

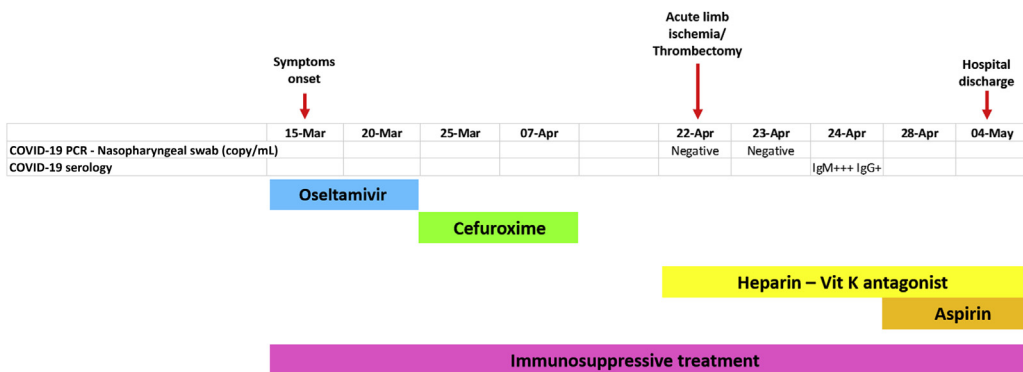


Fig 3. Patient's characteristics and results during hospitalization. COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction.

treatment was not modified considering the early onset of respiratory symptoms, absence of persistent infectious symptoms, and high rejection risk. It is impossible to know if this could have played a role in the delayed COVID-19-related vascular complications, despite initial recovery. This confirms the need to acquire new data concerning IS treatment management in SOT patients. Cohort studies and, we hope, prospective trials should help provide answers concerning these new issues.

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