

Middle cerebral artery ischemic stroke and COVID-19: a case report

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Abstract

We present a clinical case of a patient with SARS-CoV-2 infection and respiratory symptoms, complicated with a pro-thrombotic state involving multiple vascular territories and concomitant interleukin-6 increase. This case underlines the possibility to develop a COVID-19-related coagulopathy.

Keywords SARS-CoV-2 · COVID · Coagulopathy · Stroke · IL-6

Introduction

Systemic and neurological complications of SARS-CoV-2 infection are increasingly recognized. Several studies described the typical clinical presentation with fever, cough, and fatigue (Lovato and De Filippis 2020). Most recent publications (Klok et al. 2020) showed how COVID-19 might involve not only the respiratory system but also cause a pro-thrombotic state leading to peripheral veins thrombosis and pulmonary embolism. Here, we report a case of a patient with SARS-CoV-2 infection that developed severe coagulopathy affecting both pulmonary and cerebral vessels.

Clinical case

A 62-year-old patient presented to our emergency room with fever and dyspnea.

He was affected by diabetes mellitus, ankylosing spondylitis previously treated with Adalimumab and currently on Secukinumab, and complicated with pulmonary fibrosis.

He was firstly admitted to infectious diseases ward. A nasopharyngeal swab for SARS-CoV-2 resulted positive. Blood exams showed normal white blood cells with low lymphocyte levels and platelet counts, increased levels of D-dimer and lactate dehydrogenase (LDH), and slightly increased C-reactive protein (CRP). Interleukin-6 (IL-6) was also elevated (Table 1).

Therapies with oxygen, hydroxychloroquine, and prophylactic low molecular weight heparin (LMWH) were started. In the following days, the patient respiratory symptoms worsened with increasing need for oxygen therapy. Three days after admission, a marked increase in D-dimer was noted. D-dimer remained elevated in the following days (Fig. 1). Seven days after the admission, he suddenly developed respiratory insufficiency not responding to high flow oxygen administration, requiring ICU admission and mechanical ventilation. Blood exams were repeated; D-dimer was still markedly elevated; in comparison with the exams at admission, increased IL-6 (Fig. 1), severe thrombocytopenia, and only mildly increased prothrombin time and partial thromboplastin time were noted. Of interest, LDH, CRP, and procalcitonin were stable (Table 1). Two days later, at the weaning of anesthesia, the patient presented with left hemiplegia, left hemianopsia, and forced right deviation of gaze. A brain CT showed a wide infarction involving deep and superficial territories of the right middle cerebral artery and a smaller left subcortical infarction. Furthermore, a chest CT-angiography was performed, showing bilateral pulmonary embolism and confirming a severe interstitial involvement of the lungs. Ecocolor Doppler of supra-aortic vessels was unremarkable, and cardiac monitoring did not show any arrhythmias. A therapy with anticoagulant dose

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Table 1 Blood examination at admission (day 0) and at onset of pulmonary embolism (day 7). Values below or above normal limits are marked with *

	Day 0	Day 7	Normal values
WBC	$6.22 \times 10^3/\text{mm}^2$	$11.12 \times 10^3/\text{mm}^2$ *	$4.0\text{--}10.9 \times 10^3/\text{mm}^2$
Neutrophils	$5.43 \times 10^3/\text{mm}^2$	$10.46 \times 10^3/\text{mm}^2$ *	$1.8\text{--}7.7 \times 10^3/\text{mm}^2$
Lymphocytes	$0.53 \times 10^3/\text{mm}^2$ *	$0.40 \times 10^3/\text{mm}^2$ *	$1.0\text{--}4.5 \times 10^3/\text{mm}^2$
Hb	14.3 g/dl	12.9 g/dl*	13.5–17.5 g/dl
PTL	$117 \times 10^3/\text{mm}^2$ *	$68 \times 10^3/\text{mm}^2$ *	$150\text{--}450 \times 10^3/\text{mm}^2$
INR	0.90	1.29 *	0.84–1.25
D-dimer	740 ng/ml *	31,910 ng/ml *	0–500 ng/ml
Fibrinogen	491 mg/dl *	158 mg/dl *	200–400 mg/dl
LDH	1018 U/l *	1040 U/l *	230–460 U/l
Troponin	< 12 ng/l	504 ng/l*	< 34 ng/l
CRP	5.2 mg/dl*	4.1 mg/dl*	0–0.7 mg/dl
PCT	0.1 ng/ml	0.1 ng/ml	< 0.5 ng/ml
IL-6	72.10 pg/ml *	> 2300 pg/ml*	0–10 pg/ml

WBC white blood cell, Hb hemoglobin, PTL platelets, INR international normalized ratio, LDH lactate dehydrogenase, CRP C-reactive protein, PCT procalcitonin, IL-6 interleukin-6

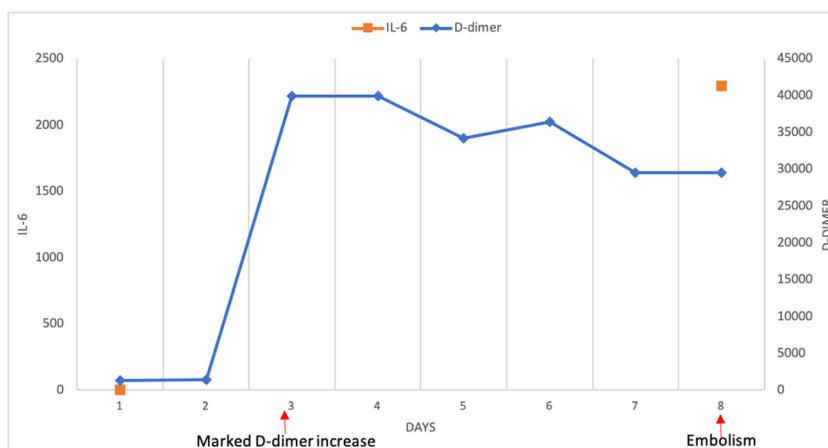
of LMWH was started. Nevertheless, the patient continued to deteriorate and died 2 days later for respiratory failure.

Discussion

Arterial and venous thrombotic events are recognized complications of SARS-CoV-2 infection (Klok et al. 2020; Beyrouti et al. 2020). The mechanism leading to SARS-CoV-2-related coagulopathy is extensively reviewed elsewhere (Iba et al. 2020). The immune system appears to play a critical role in the pathogenesis: increased levels of pro-inflammatory cytokines (i.e., IL-6), damage-associated molecular patterns release, and complement activation may trigger platelets aggregation and coagulation cascade (Iba et al. 2020). Lupus anticoagulant and anti-phospholipid antibodies have also been described in COVID-19 patients with thrombotic events

(Helms et al. 2020; Zhang et al. 2020), but a causal relation has not been proven. Finally, SARS-CoV-2 might directly target endothelial vascular cells expressing angiotensin converting enzyme 2 receptors, necessary for viral adhesion, leading to endothelial dysfunction and apoptosis with subsequent vasoconstriction, inflammation, and procoagulant state (Varga et al. 2020). Increasing IL-6 plasma concentration during hospitalization has been associated with poor outcome (Zhou et al. 2020); we report a striking increase of IL-6 concomitant with respiratory failure and pulmonary embolisms. Such finding might entail a possible pathogenic role of the cytokine storm in COVID-19-related coagulopathy, although a causative role cannot be proven and more studies are needed. Of note, severe respiratory failure was heralded by a marked D-dimer increase 5 days earlier (Fig. 1). Finally, our patient developed sudden respiratory failure with subsequent need for intubation and sedation preventing an early recognition of

Fig. 1 D-dimer and interleukin-6 (IL-6) variation in time. The line shows an important D-dimer increase 5 days before severe respiratory failure. The two dots show IL-6 level at admission and at the time of severe respiratory failure



stroke that was diagnosed only 2 days later after weaning of anesthesia. This case underlines the importance of constant neurological monitoring in COVID-19 patients during ICU staying, especially in those with suspected thrombotic events, to detect possible neurological complications. Indeed, stroke is an emerging complication of SARS-CoV-2 infection, and revascularization therapies are available, if the diagnosis is promptly done.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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