

### Concomitant brain arterial and venous thrombosis in a COVID-19 patient

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doi:10.1111/ene.14380

Received: 7 May 2020

In Revised form: 21 May 2020;

Accepted: 26 May 2020

#### Introduction

COVID-19 infection can cause severe pneumonia which, in some cases, can lead to admission to an intensive care unit for respiratory support [1]. In severe cases, systemic thrombotic complications have been described, including cerebrovascular disease (5.7%–23% of cases) [2,3].

We describe a patient with a severe form of COVID-19 who developed sudden impairment of consciousness, leading to coma. Neuroimaging suggested concomitant venous and arterial thrombosis of the brain.

#### Case report

An 81-year-old man was admitted to a respiratory semi-intensive care unit for interstitial pneumonia with respiratory distress on 25 March. Reverse transcriptase–polymerase chain reaction assay of a nasopharyngeal swab tested positive for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

The patient's medical history was relevant for ocular myasthenia, transurethral resection of the prostate for adenocarcinoma, B-chronic lymphatic leukemia and recent admission (first days of March) for hemolytic anemia treated with high-dose iv steroids and iv immunoglobulin with complete remission.

COVID-19 infection was treated with a combination of antiretroviral drugs (darunavir/ritonavir), hydroxycloquine and steroids.

During hospitalization, the patient experienced worsening of respiratory failure with necessity for non-invasive respiratory support.

A few days later, the patient experienced deterioration of his neurological condition, with mental confusion and progressive reduction of consciousness until coma on 13 April when very severe respiratory insufficiency (PaO<sub>2</sub>/FiO<sub>2</sub> < 100) was noted.

The neurological examination revealed an absence of responsiveness to pain stimulus with pyramidal signs (bilateral Babinski signs), normal pupil reflexes and periodical breathing.

Unenhanced brain computed tomography (CT) showed bilateral subacute infarcts in the middle cerebral arteries (MCAs) territory. Then, a CT angiogram of the head was performed, and bilateral occlusion of the MCAs was demonstrated; the occlusion involved the left M1 segment and the right M2 segment. A subsequent contrast-enhanced CT scan, performed with a pre-scanning delay of 40 s, showed a filling defect in the right sigmoid sinus, consistent with venous cloth (Fig. 1).

Blood analysis was not consistent with disseminated intravascular coagulation and/or multi-organ failure, while inflammatory indices dramatically increased, as typically seen in COVID-19 disease: white blood cells 59 000/mcl, lactate dehydrogenase 2466 U/l, C-reactive protein 13.62 mg/dl, fibrinogen 539 mg/dl, D-dimer 2017 ng/ml, international normalised ratio (INR) for prothrombin time (PT) 1.20, and activated partial thromboplastin time (aPTT) 26.6 s.

Unfortunately, the patient died on 15 April, despite anticoagulant treatment and non-invasive respiratory support.

Notification has been sent to the Ethics Committee of the University Hospital S. Luigi according to local rules.

#### Discussion

Our case underlines that one of the main causes for clinical deterioration and death during COVID-19 infection is coagulopathy that can involve both arterial and venous systems. In this particular case, despite the absence of clinical signs of systemic coagulopathy, there was a concomitant involvement of cerebral arteries and veins.

Unfortunately, the absence of pathological analysis at autopsy does not allow us to determine whether thrombosis was caused by large vessel vasculitis, or hypercoagulability due to antiphospholipid antibodies, that can arise transiently in patients with critical illness and various infections. This last hypothesis has been described previously in COVID-19 patients [4].

In addition, other comorbidities (leukemia) and the recent use of steroids could have influenced the pro-thrombotic status of our patient.

Acute and subacute consciousness deterioration in COVID-19 patients could be attributable to different pathogenetic mechanisms: nevertheless, acute cerebrovascular disease is the main probable cause of this deterioration, because encephalitis, for example, has been described in few case reports [2,3,5].

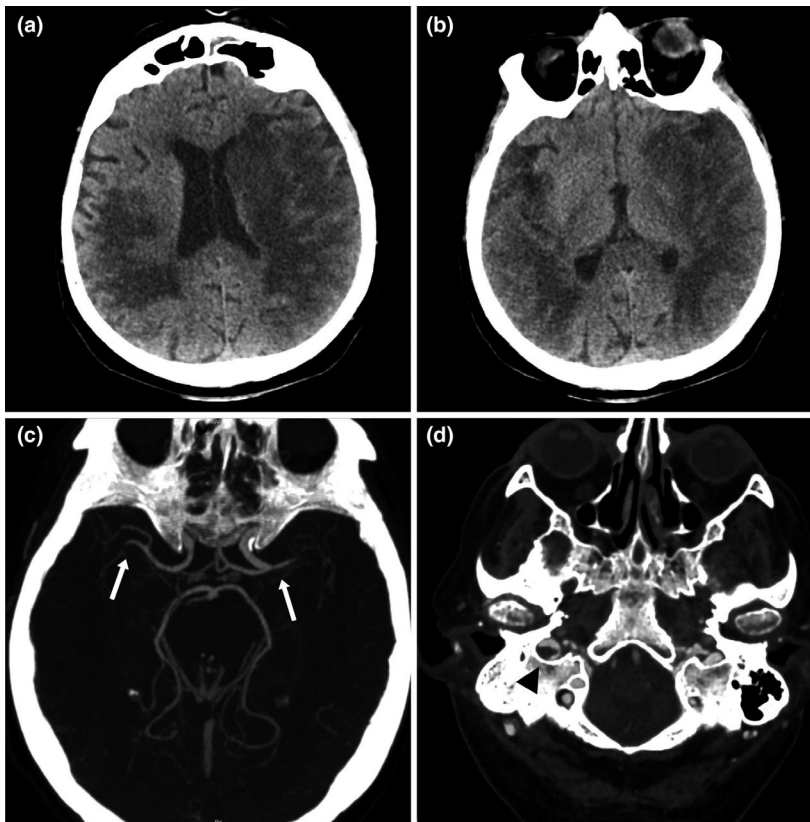
As far as we know, the simultaneous occurrence of venous and arterial thrombosis of the brain has not yet been described, and could represent an important cause of neurological impairment in patients affected by COVID-19; prompt execution of neuroradiological examination of the parenchyma and post-contrast imaging of both the arterial and venous systems could allow a correct diagnosis to be made and a more appropriate treatment strategy to be applied.

#### Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

#### Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not



**Figure 1** (a, b) Axial unenhanced computed tomography (CT) images show massive bilateral cerebral edema. (c) Maximum intensity projection (MIP) reformatted images from CT angiogram demonstrate bilateral occlusion of the middle cerebral arteries (white arrows). (d) Axial contrast-enhanced CT image (MIP) obtained with a pre-scanning delay of 40 s shows a thrombus (black arrowhead) in the right sigmoid sinus.

publicly available due to privacy or ethical restrictions.

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