



Cerebral venous thrombosis associated with coronavirus infection: an underestimated entity?

Andrea Rigamonti¹ · Vittorio Mantero¹ · Francesca Piamarta¹ · Giannantonio Spena² · Andrea Salmaggi¹

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Dear Editor,

Novel coronavirus (also called SARS-CoV-2 or COVID-19) was recently discovered in Wuhan, China. This virus has a prevailing tropism for the respiratory system; however, a number of studies have shown that coagulation dysfunction exists in patients with severe novel coronavirus pneumonia. In particular a pro-thrombotic state, with an increased incidence of venous thromboembolic events, has been reported [1–4]. A recent paper by Mao et al. [5] described the spectrum of neurological manifestations associated with SARS-CoV-2; among central nervous system manifestations, large vessel ischemic stroke has been reported in 6 of 214 cases (2.8%).

To date no cases of cerebral venous thrombosis associated with COVID-19 have been reported in the literature.

A 54-year-old male with a previous negative medical history presented to the hospital with 2 weeks of cough, fatigue and fever. On the day of admission he also complained of headache and aphasia. Vital signs on presentation were T 38.8 °C, heart rate 88 bpm, blood pressure 140/80 mmHg, respiratory frequency 22 and SpO₂ 90% on room air. Neurological examination showed non-fluent aphasia, right emianopsia and right facio-brachio-crural hemiparesis. D-dimer was 3000 ng/mL (nv < 500), reactive C-protein 9.7 mg/dL (nv < 1) and fibrinogen 936 mg/dL (nv 150–400 mg/dL). Nasopharyngeal swab was positive for SARS-CoV-2 on real-time reverse transcriptase–polymerase chain reaction assay. Chest computed tomography (CT) revealed

bilateral ground glass opacities with peripheral and basilar predominance. Brain CT showed ischaemic hypodensity involving left basal ganglia and thalamo-capsular region with a small haemorrhagic hyperdensity in the context of nucleus caudatus, associated with mass effect and shift of midline structure. An angio-CT disclosed thrombosis involving deep veins of the left hemisphere. Oxygen supplementation (15 L/min on a non-rebreather mask), hydroxychloroquine, azithromycin and lopinavir/ritonavir were started. Moreover anticoagulation (enoxaparin 100 UI/kg twice a day) and antiedema therapy was introduced.

Four days after hospitalisation, the neurological picture deteriorated and the patient became comatose (GCS 7). A brain CT showed an increase of cerebral edema and shift of midline structures. The patient was intubated and underwent surgical decompression. Despite this treatment the neurological picture did not improve and the patient died 10 days later.

Our patient did not present antecedent risk factors for cerebral vein thrombosis (i.e. malignancies, connective tissue disease, inflammatory bowel disease...) so we hypothesise that a pro-thrombotic state induced by COVID-19 infection was responsible for the development of such a condition.

A hallmark of severe COVID-19 is coagulopathy, with 71.4% of patients who died of COVID-19 meeting criteria for disseminated intravascular coagulation (DIC) [2]. Additionally, it has become clear that this is not a bleeding diathesis but rather a predominantly pro-thrombotic state with high risk of venous thromboembolism. More specifically, D-dimer, fibrinogen and fibrinogen degradation product are significantly increased, whereas AT III levels are lower in COVID-19 patients compared with a healthy control population [3]. The incidence of venous thromboembolism among COVID-19 patients in Intensive Care Unit seems to be somewhat higher in comparison with that reported in other studies including such patients with other disease conditions [4].

Over time, increasing evidence of neurologic manifestations of SARS-CoV-2-associated disease emerged. Mao et al. [5] reported that 36.4% of their 214 patients had nervous system

✉ Andrea Rigamonti
rig74@libero.it

¹ Neurological Department, “Alessandro Manzoni” General Hospital, Via Dell’Eremo 9/11, 23900 Lecco, Italy

² Neurosurgery, A.O Manzoni, Via Dell’Eremo 9/11, 23900 Lecco, Italy

related finding. These manifestations ranged from fairly specific symptoms (i.e. anosmia, ageusia, myopathy and stroke), to less specific symptoms (headache, seizure, dizziness). In this series 6 patients (2.8%) presented acute cerebrovascular disease (5 large vessel ischemic stroke and 1 hemorrhage) but no cases of cerebral vein thrombosis were observed.

It is quite surprising that, despite relevant alterations in coagulation parameters of COVID patients, no cases of cerebral vein thrombosis have been reported till now. An underestimation cannot be excluded.

Our case suggests that in COVID patients with high D-dimer and fibrinogen levels that complain headache, seizure or focal deficits, a venous angio-CT should be performed in order to exclude cerebral vein thrombosis.

Compliance with ethical standards

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

Ethical approval None.

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