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Case report

Cerebral nervous system vasculitis in a Covid-19 patient with pneumonia

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ABSTRACT

We describe a patient affected by Covid-19 acute respiratory distress syndrome with a cerebral nervous system vasculitis triggered by SARS-Cov-2, managed at the University hospital, in Novara, Italy in the area most impacted by the pandemic and where 749 Covid-19 positive patients were admitted from March 1st until April 25th, 2020.

1. Introduction

In December 2019, a new pneumonia case emerged in the Wuhan, Hubei province of China which had an association with the novel CoronaVirus (2019-nCoV) [1]. Thereafter, on the 20th February 2020, the first patient was diagnosed with COVID-19 in Italy leading to a widespread throughout the country [2] and all over the word. Clinical features vary from mild to critical symptomatic infection, mainly acute respiratory distress syndrome. Different organs, other than lung, can be involved by COVID-19 infection such as intestine, heart, kidney and brain [3,4].

2. Case report

A 64-year-old man with an history of hypertension entered in middle March 2020 the emergency department for cough and fever started 5 days before. At hospital entrance (day 0), he performed complete blood exam, nasopharyngeal swab for COVID-19 and a computerized tomography (CT) of the thorax. The blood exams showed white blood cells 6920/μL, with 1620/μL lymphocytes, ferritin 3602 ng/mL, d-dimer 581 μg/L, LDH 892 U/L, a PaO_2 59.1 mmHg in room air i.e., a ratio between partial pressure of oxygen and fraction of inspired oxygen (PaO_2/FiO_2) 281 mmHg. Nasopharyngeal swab was positive for COVID-19 and the CT-scan indicated bilateral interstitial pneumonia. He was prescribed hydroxychloroquine and Darunavir/Cobicistat and admitted to the hospital.

On day 2, his respiratory conditions deteriorated and on day 3 the patient was intubated. On the same day, low molecular weight heparin (LMWH) for deep vein thrombosis prophylaxis was started and increased to a therapeutic range on day 9. Patient was subjected to 3 cycles of prono-supination of about 18 h in deep sedation and intermittent muscle paralysis. On day 11, PaO_2/FiO_2 ameliorated, about 200 mmHg and patient started to be ventilated in an assisted mode; deep sedation with propofol and midazolam was stopped and analgo-sedation with low dose of remifentanil 0.01 μg/kg/min and dexmedetomidine 0.4 μg/kg/h started. On day 14, as patient was still unconscious, tracheotomy was performed. The electroencephalogram revealed anteriorly prominent theta and delta patterns while the head CT-Scan showed some cortical-subcortical blood-related hyperdensities in the bilateral

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fronto-parietal and right occipital lobes, leading to suspicion of subacute embolic strokes, encephalitis or cerebral vasculitis. The neurological examination revealed: tetraplegia with bilateral mute plantar response, reactive mid-size pupils, presence of corneal, photomotor, oculocephalic reflexes, no meningeal signs. GCS was 6 (E4 V1 M1). Furthermore, the magnetic resonance imaging (MRI) showed some signal restriction of the cortex in a parietal and parieto-occipital region and at the pons level suggesting both signs of cortical inflammation and ischemia in the subacute phase (Fig. 1). On the lumbar puncture examination performed on day 22, his cerebrospinal fluid (CSF) was faint yellow, with a cell count of 2/μL, glicemia 117 mg/dL, raised proteins to 91.5 mg/dL (normal values below 45). CSF array of respiratory and herpers viruses were negative as well as COVID-19 RT-PCR, while nasopharyngeal swab was still positive for COVID-19. To exclude an embolic genesis despite negative blood culture, a transesophageal echocardiography was performed.

A panel of common autoantibodies including anti-nuclear antibodies (ANA), extractable nuclear antigens antibodies (ENA), anti double strain DNA antibodies, anti neutrophil cytoplasmic antibodies was negative. Only a slight alteration of lupus anticoagulant (DRVTT) was detected but without anti cardiolipin or anti Beta2-glycoprotein detection, suggesting a false positivity as expected in critical care patients [5]. Interestingly complement fractions were very low, with C3 reduced to 10 mg/dl (normal values 10–40 ng/dl) and C4 to 4 ng/dl (normal values 90–180 ng/dl) and elevated serum beta 2 microglobulin 3080 ng/ml (normal values 900–2000 ng/ml), VES 95 mm/h (normal values 0–10 mm/h), with low level of C reactive protein 4.85 mg/dl (normal values 0.00–1.00 mg/dl) and procalcitonin 0.11 ng/ml.

According to these laboratory findings with no history of systemic autoimmune disease, a central nervous system (CNS) vasculitis was suspected. Therefore, intra-venous immunoglobulins at 30 g/die for 5 days and thereafter metilprednisolone 1 g/die for 5 days, were administered. On day 36, the patient appeared awake but unresponsive, he randomly tracked the examiner if speaking, and withdrew the left leg to pain. The remaining neurological examination was unchanged, and GCS was 9 (E4 V1 M4). MRI detected a significant reduction of the pons ischemia (Fig. 2).

3. Discussion

CNS vasculitides affect small- and medium-sized arteries of the CNS, and are rare conditions both as primary angiitis of central nervous system (PACNS) and in other systemic vasculitis [6]. Viral infections, such as Varicella zoster, West Nile, HIV and HCV viruses can trigger CNS vasculitis and PACNS [7]. SARS-CoV-2 infection in ICU has been associated to severe neurological dysfunctions and non-specific findings at brain MRI as for critical illness-related encephalopathy [3]. Moreover several mechanisms of CNS damage for by SARS-Cov-2 have been proposed including an inflammatory response mediated by cytokines such as interleukin-6 [8].

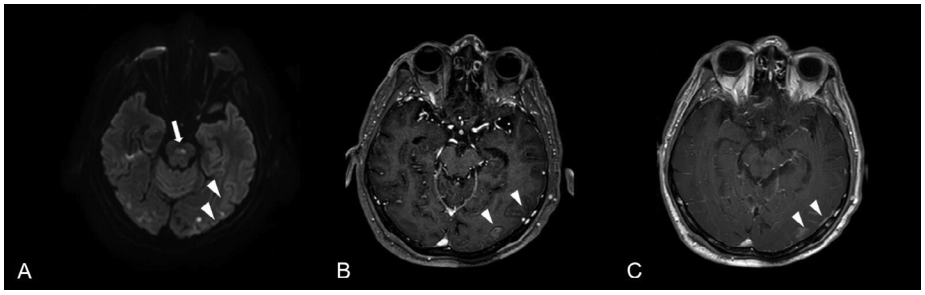

Fig. 1. (A) The DWI map detects a signal restriction of the cortex in a parietal region characterized by weak hyperintensity (arrowhead) probably due to signs of cortical inflammation. In addition, the presence of signal restriction areas at the pons level (arrow) and in the parieto-occipital area (arrow) is observed, such as for ischemia in the subacute phase. (B) The same section is performed after administration of contrast medium and reveals leptomeningeal enhancement (arrowhead). (C) Contrast enhancement was best emphasized with late acquisition after administration of contrast medium (arrowhead).

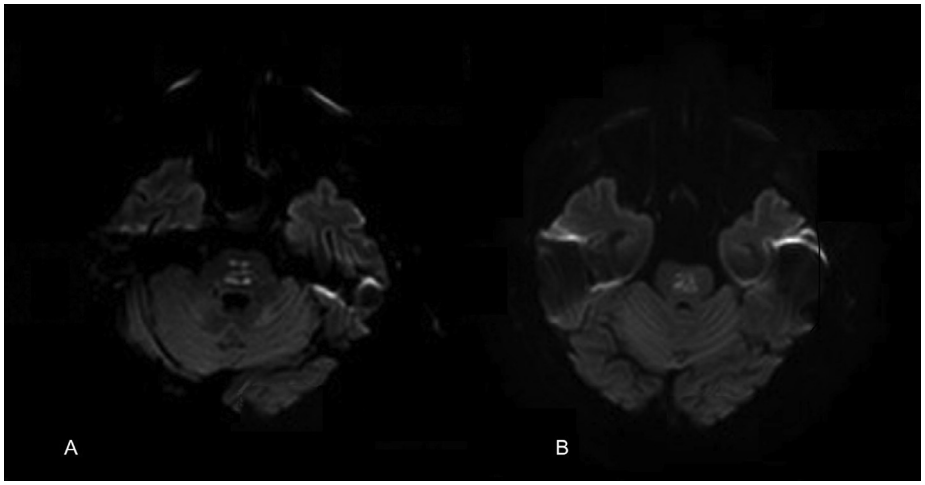

Fig. 2. The DWI maps compare two MRI sections performed on day 21 (A) and day 36 (B). A significant reduction in signal restriction is detected on the pons, consequence of a normal evolution of the recent ischemia.

4. Conclusion

In this case, the severe neurological dysfunction after SARS-Cov-2 acute respiratory distress syndrome, the pattern and load of CNS lesions at MRI, CSF findings, the clinical improvement after steroids altogether suggest the diagnosis of CNS vasculitis triggered by SARS-Cov-2 infection. Physicians should be aware of this additional severe complication associated with COVID-19.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2020.07.032.

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