CLINICAL IMAGE

Neurologic complications of SARS-CoV-2 infection in a 66-year-old man

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On March 2020, a 66-year-old man with arterial hypertension was admitted to the hospital. He presented with cough and weakness following fever (39.3 °C) and dyspnea since mid-February 2020. The real-time reverse transcription–polymerase chain reaction (RT-PCR) nasopharyngeal swab test was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On admission, the patient was in moderately good condition, with preserved cardiovascular and respiratory system function. Chest X-ray revealed interstitial inflammatory lesions (FIGURE 1A). Laboratory results showed elevated levels of C-reactive protein (29 mg/l; reference range, 0–0.6 mg/l) and D-dimer (5794 ng/ml; reference range, 0–500 ng/ml) as well as lymphopenia (0.7×10^3/μl; reference range, $1–4 \times 10^3$/μl). After 7 days of hospitalization, due to progression of inflammatory lesions in the lungs (FIGURE 1B) and exacerbation of respiratory failure symptoms, the patient was transferred to the intensive care unit.

The following drugs and procedures were used for treatment: oxygen therapy, lopinavir/ritonavir, ribavirin, chloroquine, meropenem, vancomycin, oseltamivir, low-molecular-weight heparin at a prophylactic dose, sedation-analgesia, muscle relaxants, and norepinephrine. Owing to suspected cytokine release syndrome in the course of coronavirus disease 2019 (COVID-19), tocilizumab therapy with methylprednisolone was introduced.

After 3 weeks, the patient was conscious, responsive, and spontaneously breathing. He was transferred to the internal medicine ward and received continuous neurological surveillance. At first, the patient showed illogical behavior, was delirious, and had aphasia, right hemianopsia,

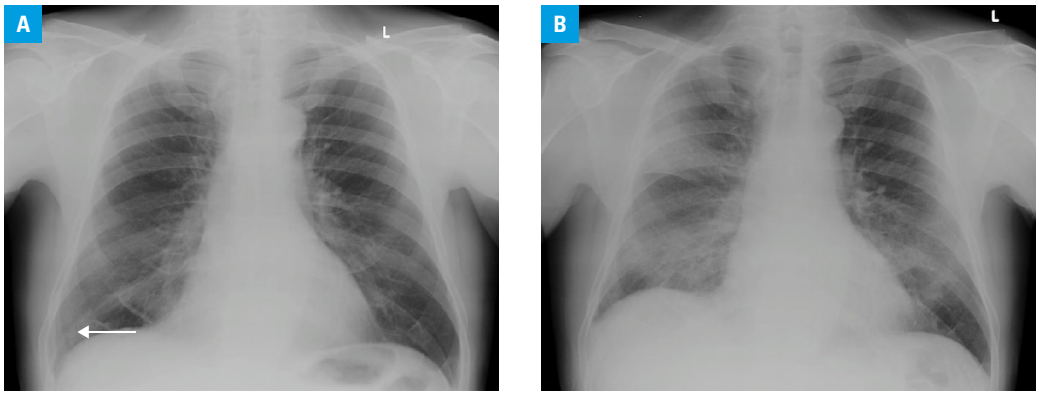

FIGURE 1 **A** – chest X-ray in the anterior-posterior projection: the intensified interstitial pattern indicative of interstitial inflammatory lesions present in the right supradiaphragmatic field (arrow); **B** – chest X-ray in the anterior-posterior projection: band-shaped and patchy densities in the central and lower right lung field and in the lower left lung field showing the progression of inflammatory lesions

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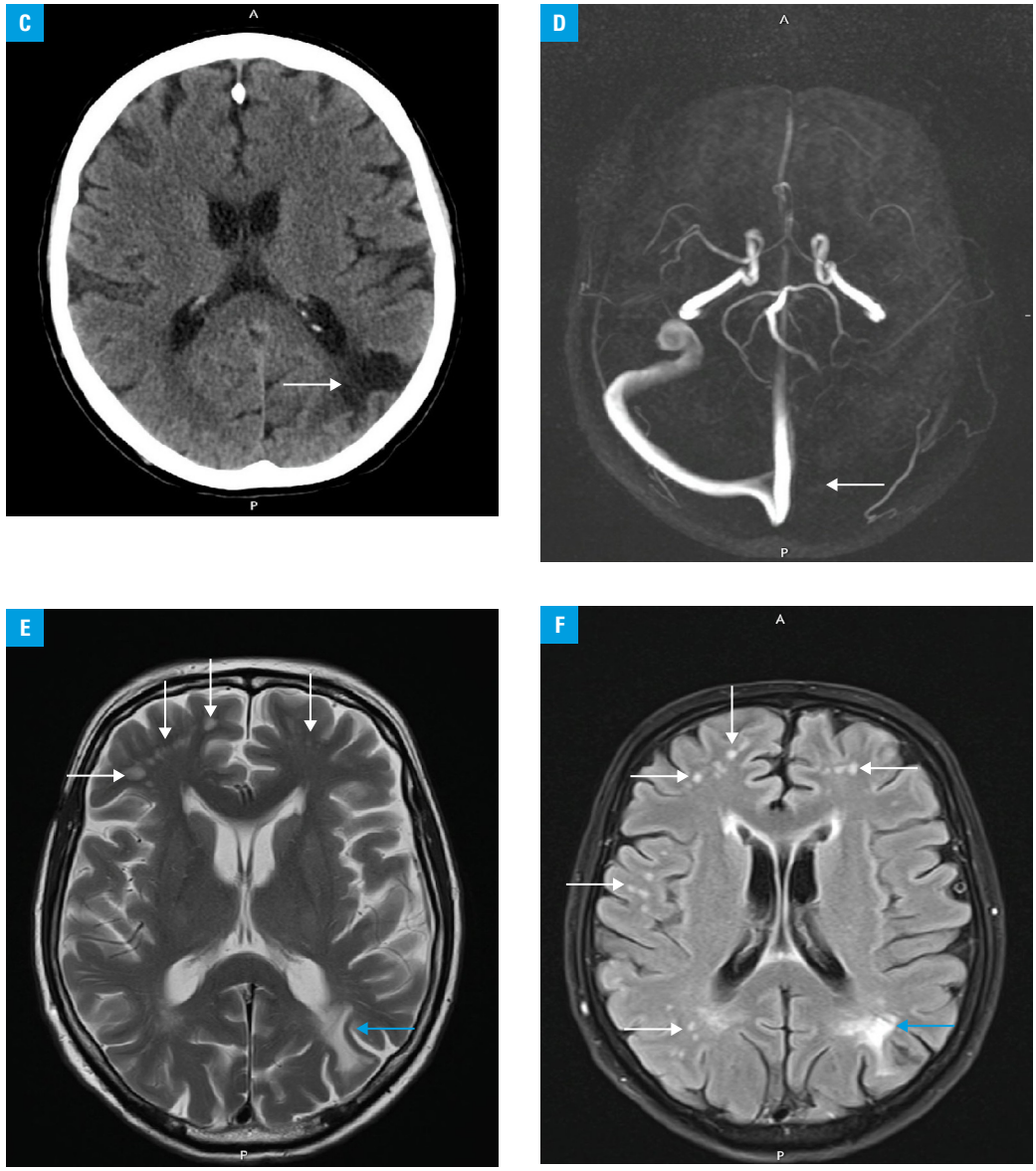

FIGURE 1 **C** – head computed tomography: a large, hypodense area (32 × 23 mm) indicative of a chronic ischemic lesion in the cortex and white matter of the left occipital lobe, involving the frontal horn of the left lateral ventricle—the focus of the previous stroke (arrow); **D** – magnetic resonance imaging angiography using 3-dimensional time of flight in the transverse plane: a filling defect in the contrasted left transverse and sigmoid sinuses, suggestive of venous thrombosis (arrow); **E**, **F** – head magnetic resonance imaging in the spin-echo T1-weighted, spin-echo T2--weighted, fluid-attenuated inversion recovery, diffusion weighted imaging sequence with an apparent diffusion coefficient, susceptibility-weighted images, and 3-dimensional time of flight map in transverse, frontal, and sagittal planes, before and after the administration of a paramagnetic contrast agent: **E** – spin-echo T2-weighted sequence in the transverse plane; **F** – fluid-attenuated inversion recovery sequence in the transverse plane. Multiple, scattered, oval and amorphous foci and hyperintensive areas can be seen supratentorially within the white matter of both hemispheres in all sites (mainly subcortically and periventricularly), indicative of degenerative and demyelinating lesions, probably of inflammatory origin (white arrows). Lesions suggestive of prior left hemispheric ischemic stroke are present in the left posterior cerebral artery territory (blue arrows).

distal flaccid symmetric tetraparesis, hypoesthesia, and painful paraesthesias of the feet. A neurologist diagnosed the patient with critical illness polyneuropathy based on movement and sensory disorders. Because of the epidemiological situation, electroneurography and electroencephalography could not be carried out. Nevertheless, due to other alarming neurologic symptoms, extensive diagnostic workup was performed. Head computed tomography showed the focus of the previous stroke in the left occipital lobe (FIGURE 1C). Computed tomography venography and magnetic resonance imaging (MRI) angiography showed cerebral venous thrombosis (CVT) of the left transverse and sigmoid sinuses (FIGURE 1D). Additionally, head MRI with gadolinium enhancement showed degenerative and demyelinating lesions without gadolinium enhancement in the white matter of both cerebral hemispheres, probably of inflammatory origin (FIGURE 1E and 1F). Cerebrospinal

fluid analysis showed protein concentration and cell count within the reference range. The RT-PCR test of cerebrospinal fluid was negative for SARS--CoV-2 yet positive for enterovirus.

Treatment involved the administration of low--molecular-weight heparin at a therapeutic dose, followed by dabigatran, pregabalin, and vitamin and protein supplementation. Rehabilitation and speech therapy were initiated.

Follow-up head MRI demonstrated a stable state of ischemic and inflammatory lesions. Follow-up MRI angiography showed complete CVT regression.

After 6 weeks of hospitalization, the patient—fully conscious and behaving logically, without visual impairment and paresthesias, able to walk with a walking frame, yet with mild speech and movement disorders—was discharged and referred for further rehabilitation.

Neurologic manifestations and complications of SARS-CoV-2 infection have been described in several reports. In a Wuhan study, 36.4% of infected patients exhibited neurologic symptoms[1]; in a Spanish report, they were observed in 57.4% of patients.[2] Symptoms of the central and peripheral nervous system and muscular involvement following SARS-CoV-2 infection have been reported.[1] The most common ones included dizziness, headache, myalgias, anosmia, and dysgeusia.[1,2]

Acute cerebrovascular diseases in the course of COVID-19 occurred in 5.7% of patients.[1] The stroke incidence of 2.5% to 6% has been reported in retrospective studies.[1] Ischemic strokes occurred mostly in older age groups and were associated with severe infection and cardiovascular risk factors such as hypertension,[3] which fully corresponds with our case. Individual cases of CVT during SARS-CoV-2 infection have also been reported.[3] Recent studies have shown the potential development of the hypercoagulable state in COVID-19. A survey from Wuhan revealed significantly higher levels of D-dimer, fibrin / fibrinogen degradation products and fibrinogen among patients with COVID-19.[4] Furthermore, in patients with severe disease, proinflammatory cytokines are released, promoting endothelial cell dysfunction and leading to excess thrombin generation and fibrinolysis inhibition.[4] This septic-like coagulopathy may also lead to venous thrombosis, ultimately disseminated intravascular coagulation.

In our case, COVID-19 was complicated by both ischemic cerebral stroke and CVT, which was a consequence of the hypercoagulable state in COVID-19, particularly common in the severe course of the disease.

In addition, the patient developed critical illness polyneuropathy as a complication of the severe course of COVID-19 and respiratory failure.[5] Furthermore, enteroviral encephalitis was diagnosed. This is the first reported case of the coexistence of SARS-CoV-2 infection and enterovirus central nervous system infection. It can be speculated that endothelial dysfunction due to SARS-CoV-2 infection enabled enteroviral neuroinvasion.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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