CORRESPONDENCE

Neurologic Features in Severe SARS-CoV-2 Infection

TO THE EDITOR: We report the neurologic features in an observational series of 58 of 64 consecutive patients admitted to the hospital because of acute respiratory distress syndrome (ARDS) due to Covid-19. The patients received similar evaluations by intensivists in two intensive care units (ICUs) in Strasbourg, France, between March 3 and April 3, 2020.

Six patients were excluded because of paralytic neuromuscular blockade when neurologic data were collected or because they had died without a neurologic examination having been performed. In all 58 patients, reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assays of nasopharyngeal samples were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The median age of the patients was 63 years, and the median Simplified Acute Physiology Score II at the time of neurologic examination was 52 (interquartile range, 37 to 65, on a scale ranging from 0 to 163, with higher scores indicating greater severity of illness). Seven patients had had previous neurologic disorders, including transient ischemic attack, partial epilepsy, and mild cognitive impairment.

The neurologic findings were recorded in 8 of the 58 patients (14%) on admission to the ICU (before treatment) and in 39 patients (67%) when sedation and a neuromuscular blocker were withheld. Agitation was present in 40 patients (69%) when neuromuscular blockade was discontinued (Table 1). A total of 26 of 40 patients were noted to have confusion according to the Confusion Assessment Method for the ICU; those patients could be evaluated when they were responsive (i.e., they had a score of –1 to 1 on the Richmond Agitation and Sedation Scale, on a scale of –5 [unresponsive] to +4 [combative]). Diffuse corticospinal tract signs with enhanced tendon reflexes, ankle clonus, and bilateral extensor plantar reflexes were present in 39 patients (67%). Of the patients who had been discharged at the time of this writing, 15 of 45 (33%) had had a dysexecutive syndrome consisting of inattention, disorientation, or poorly organized movements in response to command.

Table 1. Characteristics of the Patients with Covid-19 and ARDS.*

Variable	All Patients (N=58)
Sedation for ARDS	
Midazolam	
No. of patients (%)	50 (86)
Days of treatment	
Median	4
Interquartile range	4–7
Propofol	
No. of patients (%)	27 (47)
Days of treatment	
Median	0†
Interquartile range	1–6
Sufentanil	
No. of patients (%)	58 (100)
Days of treatment	
Median	8
Interquartile range	4–12
Neurologic signs — no./total no. (%)	49/58 (84)
Temperature >38.5°C at time of clinical examination	8/49 (16)
Positive findings on CAM-ICU‡	26/40 (65)
Agitation	40/58 (69)
Corticospinal tract signs	39/58 (67)
Dysexecutive syndrome	14/39 (36)
Brain MRI — no./total no. (%)	
Leptomeningeal enhancement	8/13 (62)
Perfusion abnormalities	11/11 (100)
Cerebral ischemic stroke	3/13 (23)§
CSF analysis — no./total no. (%)¶	
Oligoclonal bands with the same pattern in serum	2/7 (29)‖
Elevated CSF IgG and CSF protein levels	1/7 (14)‖
Low albumin level	4/7 (57)
Negative RT-PCR for SARS-CoV-2 in CSF	7/7 (100)

* ARDS denotes acute respiratory distress syndrome, CSF cerebrospinal fluid, MRI magnetic resonance imaging, RT-PCR reverse-transcriptase polymerase chain reaction, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.
† Some patients received propofol for less than 1 day.
‡ The Confusion Assessment Method for the ICU [intensive care unit] (CAM-ICU) is a diagnostic algorithm for determining the presence or absence of delirium on the basis of four features: acute change or a fluctuation in mental status, inattention, disorganized thinking, and altered level of consciousness.
§ One of the three ischemic strokes had the appearance of subacute infarcts on MRI and probably existed before SARS-CoV-2 infection.
¶ The seven lumbar punctures were performed in seven of the eight patients who underwent brain MRI and electroencephalography (one lumbar puncture was contraindicated because of anticoagulation).
‖ The patient with oligoclonal bands with the same pattern in serum and the patient with elevated CSF IgG and CSF protein levels are different patients.

Magnetic resonance imaging (MRI) of the brain was performed in 13 patients (Figs. S1 through S3 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Although these patients did not have focal signs that suggested stroke, they underwent MRI because of unexplained encephalopathic features. Enhancement in leptomeningeal spaces was noted in 8 patients, and bilateral frontotemporal hypoperfusion was noted in all 11 patients who underwent perfusion imaging. Two asymptomatic patients each had a small acute ischemic stroke with focal hyperintensity on diffusion-weighted imaging and an overlapping decreased apparent diffusion coefficient, and 1 patient had a subacute ischemic stroke with superimposed increased diffusion-weighted imaging and apparent diffusion coefficient signals.

In the 8 patients who underwent electroencephalography, only nonspecific changes were detected; 1 of the 8 patients had diffuse bifrontal slowing consistent with encephalopathy. Examination of cerebrospinal fluid (CSF) samples obtained from 7 patients showed no cells; in 2 patients, oligoclonal bands were present with an identical electrophoretic pattern in serum, and protein and IgG levels were elevated in 1 patient. RT-PCR assays of the CSF samples were negative for SARS-CoV-2 in all 7 patients.

In this consecutive series of patients, ARDS due to SARS-CoV-2 infection was associated with encephalopathy, prominent agitation and confusion, and corticospinal tract signs. Two of 13 patients who underwent brain MRI had single acute ischemic strokes. Data are lacking to determine which of these features were due to critical illness–related encephalopathy, cytokines, or the effect or withdrawal of medication, and which features were specific to SARS-CoV-2 infection.

Julie Helms, M.D., Ph.D.
Stéphane Kremer, M.D., Ph.D.
Hamid Merdji, M.D.
Raphaël Clere-Jehl, M.D.
Malika Schenck, M.D.
Christine Kummerlen, M.D.
Olivier Collange, M.D., Ph.D.
Clotilde Boulay, M.D.
Samira Fafi-Kremer, Pharm.D., Ph.D.
Mickaël Ohana, M.D., Ph.D.
Mathieu Anheim, M.D., Ph.D.
Strasbourg University Hospital
Strasbourg, France

Ferhat Meziani, M.D., Ph.D.
University of Strasbourg
Strasbourg, France

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