The need for neurologists in the care of COVID-19 patients

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Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulting in severe acute respiratory syndrome in a substantial number of patients. Approximately 5%–10% of patients need intensive care unit (ICU) admission and mechanical ventilation [1]. The primary symptoms of COVID-19 include fever, dry cough and fatigue [2]. However, a recent report from Shandong, China, disclosed that a subset of patients did not suffer from respiratory symptoms but had neurological signs and symptoms [3]. Moreover, in a retrospective study from Wuhan, China, neurological symptoms were observed in 36.4% of the hospitalized patients with COVID-19 infection and pertained to both the central and peripheral nervous system [4]. Therefore, neurologists need to be part of the multidisciplinary team taking care of the patients. Our call emerges on the one hand from evidence for the neuroinvasiveness of coronaviruses, immunopathology in animal models and observations made in previous SARS epidemics [5]. On the other hand, there is an emerging number of reports of SARS-CoV-2 infection with neurological manifestations and complications which already let us foresee the potential spectrum of disease which we will encounter in the further course of the pandemic.

The lungs are the organs most affected by SARS-CoV-2 because the virus accesses host cells via the enzyme angiotensin-converting enzyme (ACE) 2, which is most abundant in type II alveolar cells. Yet, glial cells and neurons of the central nervous system (CNS) have been reported to express ACE 2, rendering the brain a potential target of the virus [6]. Knowledge about the transneuronal transport of SARS-CoV through the olfactory bulb supports this hypothesis [7]. However, whether the viral invasion of the olfactory bulbs is the neurobiological background for smell and taste disorders reported by infected patients remains to be elucidated [8]. There is a report about a 56-year-old male in China who developed COVID-19 and in whom the virus was detected in the cerebrospinal fluid (CSF) [9]. There are no clinical details outlined beyond the information that this patient recovered and was discharged from hospital. Of note, examination of SARS-CoV-2 in CSF is not a routine examination and may not be consistently available. The concern that patients with neuroinvasive disease and atypical CNS manifestations are likely to be just a matter of time is supported by a case of COVID-19 associated acute necrotizing encephalopathy [10]. The study of the mechanism leading to neuroaxonal injury, which may involve both direct viral damage and bystander inflammation, is critical for the development of treatment strategies. Whether ACE inhibitors, which are widely used for the treatment of hypertension, suppress the adaptive immune system and the subsequent antiviral response to SARD-CoV-2 is another unsolved question [11].

The neuroinvasive potential of SARS-CoV-2 may play a role in the emergence of respiratory failure in COVID-19 patients. Indeed, coronaviruses were shown to reach the brainstem via a synapse-connected route from the lung and airways [12]. Thus, further characterization of the central cardiac and respiratory dysfunction is key to understanding the underlying mechanisms and identifying patients requiring ICU admission early. The respiratory centre is located in the medulla oblongata and the respiratory rhythm is modulated from various sites of the lower brainstem, including the pons [13]. Therefore, impaired cough and gag reflex may also indicate CNS manifestation. Still, these reflexes are associated with a considerable risk of aerosol transmission and have to be performed with caution. It is unclear if examination of other brainstem reflexes such as corneal reflexes and pupillary reflexes are helpful for early detection of CNS involvement.

Neurologists should also keep in mind the potential risks for para-infectious and post-infectious disorders. Of note, there were cases of acute disseminated encephalomyelitis, vasculopathy and Guillain–Barré syndrome in association with the Middle East Respiratory Syndrome (MERS) CoV [14]. Moreover, there is preliminary evidence for a procoagulatory state associated with COVID-19 infection and development of ischaemic stroke [15]. This needs to be considered in addition to the potential risk of cardioembolic stroke due to ACE 2 expression in the heart and subsequent cardiac dysfunction [16]. Moreover, the number of reported cases of COVID-19 patients with intracerebral haemorrhage is increasing [3]. Whether this potential association is related to uncontrolled hypertension by interaction of SARS-CoV-2 with ACE 2 needs to be clarified. Hypertensive encephalopathy may

therefore be an early sign of infection or may develop during the course. As many patients have a high body temperature and electrolyte disturbances, seizures and encephalopathy may develop. Moreover, susceptibility for more severe disease in patients with pre-existing neurological conditions and on immunosuppressive therapy is another concern. Finally, we do not know how many ICU survivors of COVID-19 will develop a post-intensive-care syndrome including crticial illness neuropathy and myopathy and suffer from long-term sequelae which again emphasizes the role of neurologists in the care of COVID-19 patients.

We therefore appreciate the concerted efforts by the European Academy of Neurology to better understand neurological manifestations and complications in order to improve the overall outcome of the pandemic and would like to raise awareness for the EANcore COVID-19 activities (https://www.ean.org/EANcore-Covid-19.4325.0.html).

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Competing interests

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