



# The Broad Spectrum of Neuro-Radiological Abnormalities in Patients Infected with SARS-CoV-2 Supports the Diagnosis of Neuro-COVID-19

Josef Finsterer

Klinik Landstrasse, Messerli Institute, Vienna, Austria

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I read with interest the review article by Kim et al. [1] about the neuroimaging findings in patients with central nervous system (CNS) manifestations of COVID-19 (neuro-COVID). I agree with the conclusions that prospective neuroimaging studies are recommended in critically ill COVID-19 patients, considering the high proportion of COVID-19 patients presenting with neuroimaging findings [1]. The study is an appealing but raises several concerns [1].

The first limitation of the study is that not the entire spectrum of neuro-COVID was encountered. As a consequence, not all characteristics of neuroimaging findings in patients with COVID-19 were discussed. Among the CNS complications of a SARS-CoV-2 infection, spontaneous angiogram-negative subarachnoid bleeding [2], multiple sclerosis [3], neuromyelitis optica spectrum disorder [4], immune encephalitis [5], Bickerstaff encephalitis (BBE) [6], reversible cerebral vasoconstriction syndrome (RCVS) [7], myelitis [8,9], cerebellitis [10], cerebral vasculitis [11], and myoclonus syndrome were not

included in this study. Imaging findings in most of these conditions are well described in the literature. However, diagnosing some of these abnormalities may be challenging. In a 26-year-old female with SARS-CoV-2 associated cerebral vasculitis, magnetic resonance imaging (MRI) revealed multiple peripherally irregularly enhanced ovoid lesions within the right fronto-parietal white matter with surrounding T2/fluid attenuated inversion recovery (FLAIR) hyperintensity suggestive of vasogenic edema [11]. In a 72-year-old female with BBE, MRI revealed hyperintensity of the right flocculus and the nodulus on FLAIR images, weak restriction of the nodulus on diffusion-weighted imaging (DWI), and linear gadolinium enhancement of the dorsal medulla on T1-weighted images [6]. In a study including ten COVID-19 patients with RCVS, conventional angiography showed moderate to severe, concentric or eccentric, multifocal narrowings of the proximal segments of various cerebral arteries [7]. These narrowings resulted in vasogenic edema, ischemic stroke, or intracerebral bleeding [7]. Cerebellitis following a SARS-CoV-2 infection in a 24-year-old male presented as cortical hyperintensity in the cerebellar hemispheres bilaterally on FLAIR, as cortical and leptomeningeal enhancement involving the cerebellar hemispheres on T1 post-contrast images, and as hyperintensity in the region of the parenchymal signal abnormalities on FLAIR and DWI [10].

A second limitation is that only CNS manifestations were included but not disorders of the peripheral nervous system (PNS) as the title suggests. Several PNS complications of COVID-19 present with imaging abnormalities, such as mono- or poly-neuritis cranialis [12], Guillain-Barre syndrome (GBS) [13], Parsonage-Turner syndrome (PTS) [14], myasthenia, myasthenic syndrome, myopathy [15], myositis [16], or dermatomyositis. Of interest for the neuro-radiologist are cranial nerve neuritis, GBS, PTS, myopathy, and myositis. In a 32-year-old male with SARS-CoV-2 infection associated with left abducens palsy, T1-weighted images of the orbita showed volume loss of the left lateral rectus muscle and T2-weighted images revealed an atrophic and hyperintense left lateral muscle [12]. Patients with GBS may show enhanced nerve roots on spinal MRI with contrast medium [17]. COVID-19 patients experiencing PTS may show an enhanced plexus lesion [14]. In a 42-year-old male with SARS-CoV-2 associated myopathy, T2-weighted MRI

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**Corresponding author:** Josef Finsterer, MD, PhD, Klinik Landstrasse, Messerli Institute, Postfach 20, 1180 Vienna, Austria.

• E-mail: [fipaps@yahoo.de](mailto:fipaps@yahoo.de)

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of the upper thigh showed marked hyperintensity in the quadriceps muscles bilaterally [15]. Myositis was diagnosed in a 42-year-old male upon clinical presentation, blood tests, and muscle MRI, showing bilateral hyperintensity on short tau inversion recovery sequences [16].

A third limitation of the study is that most of the included studies did not compare imaging results during the SARS-CoV-2 infection with those prior to the viral infection. With regard to white matter lesions, it thus cannot be determined with certainty that these lesions were not already present before the patients had COVID-19.

Overall, while interesting, the study has several limitations which challenge the results and their interpretation. These issues should be addressed to avoid drawing unsupported conclusions.

### Conflicts of Interest

The author has no potential conflicts of interest to disclose.

### ORCID iD

Josef Finsterer

<https://orcid.org/0000-0003-2839-7305>

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## Response

# Re: The Broad Spectrum of Neuro-Radiological Abnormalities in Patients Infected with SARS-CoV-2 Supports the Diagnosis of Neuro-COVID-19

Pyeong Hwa Kim, Chong Hyun Suh

Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

We appreciate the interest and the insightful comments from Dr. Finsterer regarding our article [1]. As highlighted by Dr. Finsterer, our study did not evaluate all neuroimaging findings, especially those related to the peripheral nervous system, or infrequently reported findings related to the central nervous system in COVID-19 patients [2,3]. This is likely due to our selection criteria; we excluded case reports and case series that included fewer than 10 patients, and the index test was restricted to brain CT or MRI. We appreciate Dr. Finsterer's letter that provides readers a broader perspective regarding the neuroimaging findings of COVID-19 patients.

In the present study, we focused on estimating the incidence of frequently encountered neuroimaging findings associated with COVID-19. Conservatively, an actual association between COVID-19 and the neuroimaging findings might not be conclusively assumed from only the data reported in small case series. Moreover, from a methodological perspective, it is difficult to estimate the incidence of the selected neuroimaging findings not reported in a diagnostic cohort study.

We also agree with the third limitation highlighted by Dr. Finsterer. However, we emphasize that it would be practically difficult to acquire appropriate pre-infection neuroimages (optimally, insubstantial before the infection). The majority of the included studies were retrospective; furthermore, even

in the prospective study [4], patients were enrolled after the confirmation of COVID-19. Nevertheless, among the included studies, Eliezer et al. [4] only included patients presenting with olfactory function loss for less than 15 days, and Klironomos et al. [5] also assessed previous brain MRIs when available. Furthermore, the temporal sequence is relatively clear in the studies on acute ischemic stroke [6,7]. We can at least partially assume that the neurologic manifestations reported in the aforementioned studies occurred after the infection. However, more importantly, determining whether the manifestation is causal or coincidental in such patients remains difficult.

The authors are grateful for the comments and hope that the incidence or causal relationship of the neuroimaging findings described in the letter will be further clarified in future large-scale prospective studies.

## ORCID iDs

Pyeong Hwa Kim

<https://orcid.org/0000-0003-4276-8803>

Chong Hyun Suh

<https://orcid.org/0000-0002-4737-0530>

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**Corresponding author:** Chong Hyun Suh, MD, PhD, Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea.

• E-mail: [chonghyunsuh@amc.seoul.kr](mailto:chonghyunsuh@amc.seoul.kr)