



Commentary

When is the SARS-CoV-2 infection over and what is post-COVID?

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We read with interest the article by Ahmed et al. about a meta-analysis of the neurological complications of COVID-19 patients [1]. Only studies in which neurological compromise developed after the PCR for SARS-CoV-2 became negative or studies of patients who had recovered from COVID-19 and who developed neurological disease after full recovery were included [1]. It was concluded that despite recovery from the acute infection, there may be persistent illness that requires extensive follow-up of COVID-19 patients, including those initially thought to be asymptomatic [1]. The study is appealing but raises concerns that need to be discussed.

A limitation of the study is that the inclusion criteria were based on a negative PCR for SARS-CoV-2 or the end of clinical manifestations of COVID-19 [1]. Material for PCR tests is usually taken from naso-pharyngeal swabs. However, a negative PCR test does not rule out that a patient is still infected with the virus. Although the respiratory tract is the main site of infection, there are a number of extra-pulmonary manifestations of SARS-CoV-2 infections, even at onset of the infection [2]. In addition, recovery from lung disease does not mean that the infection is over. The immune response against the virus continues even after the lung symptoms have subsided. Since many manifestations of COVID-19 are due to the immune response against the virus, considering the end of pulmonary manifestations as the end of the disease is not justified. For example, the case reported by Ishaq et al. and included in table 1, developed opsoclonus myoclonus two days after recovery from the pulmonary infection [3]. Thus, opsoclonus is not really a post-infectious phenomenon but pathophysiologically linked to the infection. The same applies to venous sinus thrombosis (VST), which occurs not only as a post-vaccination phenomenon, but also during a SARS-CoV-2 infection [4]. VST can be due to immune thrombocytopenia (ITP), which can develop as early as the pulmonary phase. However, VST may develop not earlier than after the patient had become PCR negative.

According to Table 1 there are 12 patients in whom the latency period between the COVID-19 infection and the onset of neurological disease exceeded 30 days [1]. The longest latency of the 60 included

patients was even 130 days [1]. Given these numbers, it is quite unlikely that there is a causal relation between the SARS-CoV-2 infection and the neurological compromise. These 12 patients in particular should be investigated for alternative causes of the neurological disease. Guillain-Barré syndrome (GBS) usually develops within four weeks after onset of the SARS-CoV-2 infection [5].

Another limitation of the study is that the spectrum of neurological disease after recovery from COVID-19 is broader than shown in the index study. It also includes conditions such as ventriculitis, hypophysitis, cerebellitis, brainstem encephalitis, cerebral vasculitis, or venous sinus thrombosis.

Overall, the interesting study has some limitations and inconsistencies that call their results and their interpretation into question. Addressing these issues would strengthen the conclusions and could improve the status of the study. We disagree with the notion that a negative PCR test or absence of pulmonary symptoms spells the end of COVID-19.

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Ethics approval

was in accordance with ethical guidelines. The study was approved by the institutional review board.

Consent to participate

was obtained from the patient.

Consent for publication

was obtained from the patient.

Abbreviations: COVID-19, coronavirus disease-19; PCR, polymerase chain reaction; SARS-CoV-2, severe, acute respiratory syndrome coronavirus-2.

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Availability of data

All data are available from the corresponding author.

Code availability

Not applicable.

Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval, DM: literature search, discussion, critical comments, final approval.

Declaration of competing interest

None.

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