Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19-related autoimmune disorders of central nervous system (CRAD-C): Is it a new entity?

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Dear editor

Since the outbreak of the COVID-19 pandemic in December 2019, it has quickly become clear that this new disease can affect many organs, along with the lungs too. Accordingly, one of the first organs reported to be involved, was the central nervous system (CNS). This involvement takes place in different ways. The severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*) itself can cause anosmia or encephalitis by directly involving the olfactory nerves or brain tissue, respectively [1]. However, one of the main characteristics of this virus is its immunogenic characteristic, which by involving different parts of the body, including different areas of the CNS, can cause many autoimmune disorders [2]. Despite numerous studies conducted on autoimmune diseases following COVID-19, there still are many questions about the nature of these disorders. Especially, this question should be answered whether COVID-19-related autoimmune disorders of the CNS (CRAD-C) is a new entity or not.

The development of autoimmune diseases following an infection is a well-known topic. Therefore, this issue is not far-fetched in case of the COVID-19 disease. Numerous and various reports have been published on inflammatory diseases of the CNS following the development of COVID-19, which indicated this issue and mainly considered it as an immunological reaction to COVID-19 [3]. In addition, it has been treated using the same way in similar cases. However, it should be noted that the role of viruses in the pathogenesis of a neuroinflammatory disease goes beyond this. Currently, we know that viruses play an important role in the pathogenesis of some diseases such as multiple sclerosis [4] and even neuromyelitis optica spectrum disorder (NMOSD) [5]. As well, there have been reports of these diseases after developing COVID-19, suggesting that the SARS-CoV-2 may also be involved in their pathogenesis [6,7]. However, the association between the SARS-CoV-2 and neuroinflammatory diseases seems to go beyond these two known roles of viruses in the pathogenesis of these diseases. Moreover, there have been reports of co-infection of COVID-19 with MS [8], as well as between COVID-19 and autoimmune encephalitis [9]. These reports in which the patient had simultaneous manifestations of both diseases indicated a prominent role of the coronavirus in the development of these diseases. The reported cases were treated in the same way as those diseases with no specific cause. But, we do not know if, in the long-run, the course of these autoimmune brain diseases associated with COVID-19 is similar to those developing without any association with COVID-19.

This question can possibly be answered only with long-term follow-up of these diseases. There are reasons to believe that we are dealing with a different entity in case of inflammatory diseases related to the CNS. Currently, we know that COVID-19 is not a transient infection; however, its symptoms can continue for a long time [10]. In addition, there have been reports of a possible role of this virus in causing neurodegenerative diseases. The fact that this virus can cause a hyperferritinemia [11] is considered as one of the reasons for this virus's role in initiating the neurodegenerative process. It should be noted that iron deposition in the brain is an important cause of the degeneration process [12]. This evidence along with the vast neurological manifestations of COVID-19, as well as its different roles in the development of inflammatory diseases of the CNS, all raise the suspicion that this group of diseases associated with COVID-19, may subsequently form a new separate entity, though the exact answer to this question requires performing more and studies with longer follow-ups on these patients.

If CRAD-C would be considered as a distinct entity, the long-term maintenance treatment may be mandatory. As mentioned earlier, the coronavirus is not only immunogenic, but it also appears to be a stimulus for neurodegenerative processes with some lesser-known mechanisms. Therefore, the initiation of maintenance therapy in these patients should be seriously considered. Accordingly, this can prevent the disease from progressing in the future.

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