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Letter to the Editor

Causality between SARS-CoV-2 and multiple sclerosis remains unproven

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Letter to the Editor

With interest we read the article by Palao et al. about a 29 years-old female who was diagnosed with SARS-CoV-2 triggered multiple sclerosis (MS) based upon right-sided optic neuritis and two lesions, one in the right occipital region and one in the left temporal area [1]. The occipital lesion enhanced upon contrast medium [1]. It was speculated that "an immune mechanism induced by SARS-CoV-2, which can activate lymphocytes and an inflammatory response, play a role in the clinical onset of MS" [1]. The study is appealing but raises comments and concerns.

We do not agree with the diagnosis MS. Though there are two separate cerebral lesions (dissemination in space) of which one was enhancing, there is no dissemination in time, which is required for diagnosing MS according to the 2017 McDonald criteria. Furthermore, no convincing data were provided that unequivocally excluded all differential diagnoses of MS. The main differential that needs to be excluded is acute, disseminated encephalomyelitis (ADEM). Optic neuritis may not only indicate MS but may be also associated with ADEM [2]. Oligoclonal bands (OCB) can be transiently also positive in ADEM [3]. Since ADEM is usually monophasic and relapsing-remitting MS polyphasic, it is crucial to know the long-term outcome of the index patient.

Other differentials that need to be excluded are cerebral inflammatory vasculopathies (neuro-Behcet, systemic lupus erythematosus, Sjögren syndrome, granulomatous polyangitis (Wegener disease), sarcoidosis, anti-phospholipid syndrome, paraneoplastic syndrome, cerebral vasculitis), infectious diseases (borreliosis, HIV encephalitis, progressive, multifocal leukoencephalopathy (PML), neuro-syphilis, neuro-cysticerkosis, toxoplasmosis, tuberculosis), CADASIL/CARASIL, Fabry's disease, Susac's syndrome, metastatic tumors, multifocal gliomas, and primary CNS lymphoma. Since the "central vein sign" may be helpful to delineate MS from cerebral, inflammatory vasculopathies [4], we should know if the two cerebral lesions were located perivenularly or not.

A further shortcoming is that a causal relation between SARS-CoV-2 and optic neuritis and the cerebral lesions was not confirmed. The index patient was not tested positive for SARS-CoV-2 by a PCR test, neither in the cerebrospinal fluid (CSF) nor on a naso-pharyngeal swab test. Though her father was infected by SARS-CoV-2, though she experienced transient ageusia and hyposmia, and though IgG and IgM antibodies against SARS-CoV-2 were positive in the index patient, this does not necessarily mean that SARS-CoV-2 was responsible for optic neuritis respectively the cerebral lesions. Helpful in this respect would be cerebral MRIs recorded prior to the suspected SARS-CoV-2 infection. If the two lesions were present already prior to an eventual SARS-CoV2- infection, a causal relation seems unlikely.

Missing is a discussion about the increasing evidence for cranial nerve involvement, including the optic nerve, in SARS-CoV-2 infections [5]. In a recent review of 56 SARS-CoV-2 infected patients with cranial nerve involvement, the optic nerve was unilaterally affected in 7 of these patients.

Overall, the interesting study has a number of shortcomings, which should be addressed before drawing conclusions as those presented. The diagnosis “MS” should be revised, the causal relation between SARS-CoV-2 and the clinical findings should be established, evidence should be provided that all differentials of MS were excluded, and optic neuritis without MS should be discussed as a complication of SARS-CoV-2.

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There are no conflicts of interest.

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